

GOLD THERAPY IN PULMONARY TUBERCULOSIS.

A Study of the Literature with
Observations on 24 Cases treated
personally.

A Thesis

by

Charles Patrick Hay, M.B., Ch.B.

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Biëtt, Lallemand (7), Wendt (8), Le Grand (9), Eberle and Kopp. Majendie (10) declared his firm belief that the cyanuret of gold promotes coagulation of the blood. When, therefore, a decided modification in this fluid is desired in haemorrhages or in chronic affections, its administration may prove of great benefit. M. Chavannes (II) has found the chloride of gold to be a remedy of rare virtue when applied externally as a caustic in lupus, syphilitic tubercles and ulcers.

Orfila (12) affirms that the chloride of gold is more active than corrosive sublimate, and that when administered in doses of 1/20 to 1/10 gr. it will give rise to more or less inflammation of the gastro-intestinal mucous membrane.

Experiments on dogs go to prove that even when a very small amount of this preparation of gold in solution is injected into the jugular vein, death will speedily ensue by vomiting and suffocation, preceded by a short paroxysmal cough.

In 1837, Le Grand published observations on 35 cases of cure obtained by the use of gold or its preparations in the treatment of scrofulous diseases of the glands and other soft parts.

Since the proof of the infectious nature of tuberculosis by Villemin in 1865, and the discovery of the tubercle bacillus by Robert Koch in 1880, there have been numerous efforts to find a chemo-therapeutic remedy for tuberculosis. As is well known there are two great difficulties - the fatty or waxy envelope of the tubercle bacillus and the scanty blood supply of tuberculous lesions.

Already in 1890, Koch had shown that $K Au Cy_2$ is an extremely powerful bactericide to the tubercle bacillus. Subsequently von Behring showed that the concentration of 1/1,000,000 of $K Au Cy_2$ was sufficient to prevent the growth of the tubercle bacillus in culture media, but that in the presence of serum the growth preventing concentration was reduced to 1/25,000.

Previous to the introduction of sanocrysin, various attempts were made to treat human tuberculosis by the injection of gold salts. An account of their preparation and a criticism of the results obtained, is to be found in Moellgaard's book on sanocrysin (15), where he advances arguments to explain the failure of $K Au Cy_2$ etc., to cure human tuberculosis.

Moellgaard based his researches on the chemo-therapeutic principles of Ehrlich. He synthesised a gold salt with the formula $(S_2O_3Au) Na_2S_2O_3$, which he called sanocrysin, and the first clinical trials with this substance were begun by K. Secker in November 1923.

Moellgaard gives a full account of the physical, chemical and bacteriotropic properties of sanocrysin. He cites experiments on calves and smaller animals to show that sanocrysin injected intravenously in a concentration of 1/75,000 to body weight has no injurious effect on the healthy animal, but has most remarkable effects on the tuberculous organism. He has the following three groups of experiments to prove that sanocrysin exerts a direct bactericidal effect on the tubercle bacillus.

(1) Researches into the influence of sanocrysin on the

growth of the tubercle bacillus in culture, showing that sanocrysin in a concentration of 1/100,000, inhibits the growth of T.B. bovinus in cultures, without killing all the bacilli; in a concentration of 1/1,000,000, it has some inhibitory effect.

(2) Study of the influence of sanocrysin on the morphology and staining properties of the tubercle bacillus in culture, showing that a 1/10,000 solution of sanocrysin injures the acid-fast properties of T.B. bovinus.

(3) Researches into the ability of sanocrysin to prevent artificially infected guinea-pigs from getting generalised tuberculosis, which resulted in four out of five treated guinea-pigs escaping generalised tuberculosis, whilst the five control guinea-pigs contracted generalised tuberculosis.

Before considering Moellgaard's later experiments on tuberculous animals it must be understood that Moellgaard was convinced that he had in sanocrysin a direct bactericide to the tubercle bacillus. His interpretation of the experiments and the theory of sanocrysin therapy that he has built up were based on that assumption. At the same time he regards these experiments as the strongest indirect evidence that sanocrysin destroys tubercle bacilli in vivo and liberates their toxins. Moellgaard believes that sanocrysin injected into a tuberculous mammal, may cause symptoms in three ways:-

(1) Tuberculous toxæmia, due to the liberation of endotoxins or destruction of tubercle bacilli; febrile reactions and loss of weight being ascribed to this cause;

(2) "Sanocrysin shocks" due to the formation of a toxin under the influence of the tuberculin released by destruction of tubercle bacilli, and to the failing immunity of the animal to this toxin;

(3) Tuberculin reactions, which may take the form of focal reactions in any part of the body which is infected with tuberculosis.

Bang (17) attacked Moellgaard's whole position, his main points being:-

(1) Sanocrysin, in a concentration of 1/3,200, does not inhibit the growth of tubercle bacilli in cultures (Dixon (18) thinks that this was due to the presence of protein in Bang's experiments);

(2) Sanocrysin in a 1% solution is incapable of killing tubercle bacilli in eleven days;

(3) Sanocrysin has no curative power on experimental tuberculosis in rabbits;

(4) Moellgaard's anti-toxic serum cannot be in any way specific, for it is incapable of protecting tuberculous guinea pigs against genuine tuberculin shock, provoked by the injection of the smallest lethal dose of tuberculin. Moellgaard (19), in reply to Bang, argues that sanocrysin may be a real bactericide in vivo, even if its action is variable in vitro; also sanocrysin may fail to cure tuberculosis in rabbits, and still be effective in the treatment of other mammals.

Sir A. Wright (20) found that sanocrysin dilutions of 1 in 250 are without effect on tubercle bacilli in blood, and Moellgaard has admitted, that the nature of culture

and medium have an important influence on the inhibitory power of sanocrysin (21), and quotes further experiments; "In my first experiments I found the growth preventing concentration to be 1/100,000. The same has been found in two German Laboratories. But in recent times Madsen of the Serum Institution of the Danish State has found rather big variations in the growth preventing concentrations. It appears that the lowest growth preventing concentration has been found in the case of a culture taken directly from the sputum, and that laboratory cultures accustomed to sprout on artificial media seem to be generally more resistant".

One chapter of Moellgaard's book records the results of his experiments with sanocrysin on sound animals. Reference has been made to his claim that sanocrysin, injected intravenously in amounts not exceeding 1 c.gm. to each k.g.m. of body weight, has no injurious effects on the animals tested. However, the experiments show that larger doses tend to produce albuminuria, and in the case of the guinea-pig, tubular nephritis. No pathological changes were ever observed in the liver, even following very large doses. The excretion of sanocrysin, according to Moellgaard, is chiefly by the kidneys. Gold is found in the urine of a healthy calf for four to six days after the injection of 1 g.m. of sanocrysin and traces of gold are present in the faeces twenty-four hours after the final injection of sanocrysin (total amount injected 17.25 g.m. in twelve weeks) showed the following amount of gold in the organs analysed:-

Kidneys	- 0.71 gm.
Liver	- 0.13 gm.
Lungs	- 0.05 gm.
Small intestine, caecum, colon and intestinal contents.	- traces only

Gold differs from many other heavy metals in that it is excreted mainly by the kidneys, instead of the intestinal canal. No doubt Moellgaard was aware of this, but he appears to have overlooked two other remarkable facts.

In 1918, De Witt (31) and others investigated the distribution of gold and other metals in animal tissues.

Gold seems to select the spleen by preference. This organ contains four times as much gold in proportion to its weight as the liver or kidney - sometime the kidney and sometimes the liver comes second in gold concentration. About half the gold administered has been recovered from urine and faeces, a week after a single injection. More is excreted by the urine than by the faeces, at least after the earlier injection. A considerable amount of gold was recovered from the red blood cells, two to four hours after an intra-muscular injection; twenty four hours later, none was found. The exact distribution of sanocrysin in the healthy human body is not known; probably it does not differ much from the proportion found in the organs of tuberculous persons who have died after sanocrysin treatment.

Elliott (32) found that sanocrysin was rapidly excreted by the kidneys and to a less degree by the intestine. Langmead (33) found 4.75% of the total gold salt injected, in the liver; there was only one hypertrophied kidney which showed tubular nephritis; the kidney was not analysed for gold. The patient had been treated with sanocrysin and serum; jaundice was present nineteen days before death. Elliott (34) examined the kidneys and liver of a patient who died after receiving 4 gm. of sanocrysin in eleven days, with 300 cc. of serum. The kidneys contained 8% of the total gold salt injection, the liver contained only about 0.12%.

McCluskey and Eichelberger (35) have studied the results of the intravenous injection of sanocrysin on normal dogs. There is a full account of the distribution of gold in the organs at varying intervals after the final injection. Immediately after an injection, the great bulk of the gold is recovered from the kidneys.

Eight days after the disappearance of gold from the urine a small amount persists in the kidneys and spleen, approximately equal in proportion to the weight of the organs. The conclusions of these workers are as follows:

(1) The percentage of recovery of gold from the urine is practically 60%

(2) Albumin, varying in amounts from a trace to 1.2 gm. per litre, was observed in all cases. The albumin -

uria increased with increased dosage and lasted for a period of from four to ten days with subsequent re-appearance.

(3) The intravenous injection of the gold compound in the doses used in dogs caused diarrhoea and oliguria and seemed to affect the vomiting centres. The vomitus contained much bile but no gold.

(4) The excretion of urea, chlorides and creatinine in the urine was decreased following an intravenous injection of sanocrysin.

(5) Three to five per cent of gold was excreted through the intestine during the first week after the injection of sanocrysin.

(6) The intravenous injections of sanocrysin have no effect upon body temperature.

(7) The greatest amount of gold from sanocrysin localised in the organs at any time does not exceed 32% of the amount injected.

(8) Gold appears in the urine thirty minutes after an intravenous injection of sanocrysin.

Clinical trials with sanocrysin were begun in November 1923, in several Danish Hospitals and Sanatoria (22). It appeared early that the drug was useless in "surgical" tuberculosis and dangerous in advanced phthisis. In spite of many disasters, 136 cases of pulmonary tuberculosis had been treated by the latter end of 1924; 21 of them died as a direct result of treatment and several

others died subsequently. The common causes of death were hyperpyrexia, shock and cachexia. Dr. Faber, Professor of Medicine at Copenhagen University began to treat phthisis with sanocrysin in September 1924, and quickly discarded the method of administration which had been employed up to that time. Two among his first patients died, one of hyperpyrexia and one of shock. After observing these two cases Prof. Faber decided to lengthen the time interval between the doses and to begin with very small doses in severe cases. In July 1925, he was able to say that he had treated 32 cases of phthisis in the past six months without a fatality, and in many instances with astonishing improvement (23). His main principles of treatment were as follows:- (1) Dosage: 0.5 gm. for the first dose and 1 gm. for subsequent doses, increasing gradually. (2) Interval between doses: three days between the first and second doses and five days between the later doses, and if a dose caused a reaction, the treatment was to be suspended until all signs of reaction disappeared. (3) The use of Moellgaard's anti-toxic serum, which in itself caused troublesome and confusing reactions was limited to severe cases. (This serum was obtained from calves which had been 'immunised' by injections of killed cultures of tubercle bacilli). (4) Extensive cases of febrile phthisis were not to be treated.

The clinicians, who collaborated in Moellgaard's book, published preliminary results in 1924 (24). The number of cases treated was 136 with the following results:-

Free from symptoms	25
Improved	30
Uninfluenced	41
Exacerbated	19
Died	21

The preliminary report of the British Medical Research Council covered the immediate results of treatment in about 30 cases, of whom 22 definitely had tuberculosis of the lungs. Of these 22, 4 died, 4 were worse, the condition of 5 was unchanged and 9 showed improvement.

Results published in July 1925, by Faber (25) were more promising.

On January 12th 1926, there was a discussion on sanocrysin at the Royal Society of Medicine. Prof. Elliott had treated 11 cases: he believed that sanocrysin produced quicker improvement in pulmonary tuberculosis than did any other treatment.

Prof. Lyle Cummins thought that sanocrysin gave rise to definite improvement but that repeated short courses would be found to be necessary.

Prof. F.R. Fraser considered it doubtful whether the advantages of the treatment outweighed the dangers.

Permin (26) has tried sanocrysin in a number of desperate cases of advanced phthisis. In the majority the treatment had to be abandoned, but he states that 10 cases were improved, some of them considerably.

Lehotay (27) considered that sanocrysin is contraindicated in severe cases where the Pirquet reaction is negative, and a very great rate of sedimentation of the red blood cells is present.

Czerny and Oppitz treated 12 cases of tuberculosis in young children and infants; 3 children had tubercular meningitis, 3 miliary tuberculosis and 6 advanced pulmonary tuberculosis. Eleven of the 12 died, and the twelfth patient did not improve. These writers conclude that sanocrysin is useless in the tuberculosis of young children.

Prof. Friedmann (28) of the Virchow Hospital, Berlin, and others have treated 54 cases of pulmonary tuberculosis with sanocrysin. Ten were very much improved. Various methods of dosage were used: four cases were treated with massive dosage by Secker's method, and they all died. After this, Secker's method was abandoned and small doses, gradually increased were employed (0.1 gm., 0.2 gm., 0.3 gm. etc). Prof. Friedmann says "We believe that the improvement in many cases was more remarkable than any we have obtained by older methods of treatment - - fresh exudative cases offer a special field for sanocrysin therapy." K. Herius (29)

treated nine severe cases. His general opinion of the treatment is distinctly favourable, but the necessity for selection of cases is emphasised.

Opinions as to dosage began to alter about this time. The large doses advocated by Prof. Moellgaard and Dr. Secker had been widely used, with short intervals between doses. Given the right type of case this heroic line of treatment was effective; but the cases capable of standing such intensive treatment are rare and the results were often alarming and sometimes regrettable. There occurred on the one hand, high temperatures, marked albuminuria, extensive morbilliform or scarlatiniform eruptions, nausea and vomiting, loss of appetite and loss of weight, sometimes followed by a rapid and dramatic improvement after the initial course of treatment; or, on the other, the patients might show a dangerous drop of temperature, "shock" with the signs of oedema of the lungs, marked and persistent anorexia, or rapid wasting and cachexia, sometimes leading to death within a few weeks in cases which had before treatment seemed destined to a fairly long survival.

As a result of these severe reactions, smaller doses began to be given, with longer intervals between doses and avoidance of the anti-tubercular serum, which, while said to be effective in "shock" was in itself very trying to the patients and quite unnecessary if "shock" could be avoided.

S.L. Cummins (39) advocated an initial course of 0.25 gm. 0.5 gm. 0.75 gm. 1 gm. 1 gm. 1gm., the doses being separated by intervals of about seven days.

Even during a course of this description it was usual to have considerable reactions after the second third and fourth doses, albuminuria, rash or sore mouth.

It was found, however, that given in this manner that a tolerance to increasing doses was soon observable.

Moellgaard's original experimental work began also to be very closely criticised, and his contention that sanocrysin acted as a 'steriliser' of the tubercle infected organism was shown by several workers to be untenable.

Sweany and Wasick (40 & 41) repeated Moellgaard's work on the effect of the tubercle bacillus in vitro. Varying concentrations ranging from 1:1,000 to 1 & 1,000,000 were made up in 2% glycerinated agar, and these tubes were inoculated with a culture that had been on artificial medium for years although it was highly virulent for guinea pigs. There was a definite blackening of the bacilli in all dilutions up to and including 1-20,000 that appeared in about 12 days. There was complete inhibition up to 1-200,000 a partial inhibition up to 1-500,000, and slight inhibition in 1-1,000,000.

The process was repeated with an old bovine culture with identical results, but a more freshly-isolated

human strain behaved a little differently. There was not the intense blackening and a few colonies grew in concentrations as low as 1-20,000, but died out after forty days. These results, although slightly, ^{less} favourable than those of Moellgaard, may be said to coincide with his inhibitive experiments in glycerine-bouillon.

So far, therefore, as artificial medium was concerned the product was all that could be desired, but when the reaction was transported to animal body fluids, numerous complicating factors arose.

Von Behring (42) pointed this out in working with gold cyanide. In artificial medium, gold cyanide inhibited growth in 1-1,000,000 dilution, but in serum the inhibition decreased to 1-25,000. Sweany and Wassick found, however, that 5% horse serum in a glycerinated bouillon did not decrease the inhibitive results, because no growth at all was obtained in 1-1,000,000 concentration of sanocrysin. Bactericidal experiments were next performed by exposing measured quantities of tubercle bacilli to varying concentrations of sanocrysin in salt solution and serum for periods up to forty eight hours. Bacilli exposed to concentrations of 1-1,000, for two hours grew on Petroff's medium almost as well as the controls.

Small doses of bacilli (about 20,000 per c.c) exposed for forty-eight hours in a concentration of

1-5,000 sanocrysin in human serum, produced slightly less tuberculosis in guinea pigs than the controls. The difference though not marked was definite.

It was next determined whether the bacilli were killed with the salt over long periods of exposure by injecting into guinea pigs the original bouillon cultures after sixty days incubation. It was found here, again, that the organisms survived in 1-2,000 concentration for this period of time sufficiently to produce a typical tuberculosis. The altered organisms recovered were quite virulent to guinea pigs.

Various experiments were then performed to determine the effect of the salt on the morphology and staining of the bacillus. It was found that the blacking of the bacilli was apparently a deposition of the gold in the granular portions of the bacilli, and that this did not occur in dead bacilli. As the older organisms have a greater tendency to granule formation, it would follow that this form is the one in which the gold is deposited most readily.

The authors conclude that sanocrysin inhibits the growth of the tubercle bacillus in vitro, but rapid bactericidal power is practically nil. The effect appears to be to alter the organisms, but not to decrease materially their pathogenicity for guinea pigs.

This evidence, then as will be discussed below, sets at naught the theory of "tuberculin shock" that follows

the injection in patients. This 'shock effect' is more probably due to a poisoning of the endothelium (or modified endothelium) as pointed out by Huebner (43).

Jensen (44) also points out that a negative finding of tubercle bacilli in sputum of a sanocrysin case does not necessarily indicate that bacilli are absent, but may be due to the fact that they are decolorised by ordinary methods.

These experiments on the bactericidal powers of sanocrysin show then, that Moellgaard's original claim that the drug actually penetrates tuberculous lesions, which are not rendered impenetrable by fibrosis, and kills the enclosed tubercle bacilli, can no longer stand. An interesting experience of Wirz (45) has some bearing also on this point. In two cases of haematogenous skin tubercles which he treated with intravenous injections of related gold compounds (aurophos and lopion) new skin lesions appeared during the course of treatment.

Lydia M. De Witt (46) experimented with various gold cyanides in tuberculous guinea-pigs, and in 1917 reported the significant observation that tubercles flourished in the liver, spleen, lungs and other tissues even though the concentration of gold in these tissues was much more than needed to prevent the growth of the tubercle bacillus in the test-tube. To explain the failure of the substance to act in vivo she suggested such possibilities as a transformation of the chemical in the tissues into an inert

form, protection of the bacilli by peculiarities of their own structure or their cellular environment, or a tolerance acquired by the bacilli for gold.

The proponents of sanocrysin explain its alleged superiority on the basis of a diffusibility greater than that of such salts as the cyanides. Practically speaking, however, the important point is that there has been no conclusive proof of the ability of injected sanocrysin to kill tubercle bacilli in diseased animals and that the available evidence is decidedly against such an hypothesis.

In human pulmonary cases evidence of considerable weight in relation to this allegedly specific effect should be obtained from a study of changes in the bacillary content of the sputum. Many clinicians have stressed this feature, Koch (47) for example, reports that 39 of 78 sanocrysin-treated patients lost tubercle bacilli from their sputum, while a like change occurred in only 7 of 65 "control" cases. Many of his treated cases lost their bacilli after two to five doses of the drug. This would seem to argue strongly for a sterilizing effect, but a close examination of Koch's results shows that he depended on the microscopical examination of single sputum smears. In view of the work of Sweany, Wasick (40 & 41), Jensen (44) and Amberson, McMahon and Pinner (48) this cannot be taken to mean that the sputum is free from virulent tubercle bacilli. These latter authors in twelve carefully controlled cases, with cultural and inoculation methods of examin-

ing the sputum, found no evidence whatever that sanocrysin had a sterilizing effect on the living human tuberculous organism.

In the earlier experimental and clinical investigation of sanocrysin, the tendency was to attribute almost all the by-effects of the drug to the liberation from killed bacilli of tuberculous toxins into the blood stream. The assumption was based largely on the observation that the toxic signs present themselves much more promptly and severely in tuberculous subjects than in normals. Since this time evidence has accumulated to show that a good many of these manifestations are not to be explained as "tuberculin-effects"; but as the direct symptoms of metallic (gold) poisoning. Nevertheless, there is reason to believe the drug actually does in some tuberculous cases elicit certain responses which are closely analogous to those produced by the introduction of tuberculin. An intensely acute inflammatory reaction about pre-existing tuberculous foci in the lungs of man and animals treated by sanocrysin has been demonstrated by Moellgaard, and this bears every resemblance to the "tuberculin Pneumonia" of Virchow. In clinical cases receiving sanocrysin, it is easily possible to attribute the rapid break-down and excavation of old tuberculous deposits, as well as their peripheral spread, to a similar mechanism. Constitutional symptoms, such as fever, also may fit into this picture. Since a tuberculin-like effect may, therefore, be an actuality and since there is very slender evidence that this

could be due to the killing and disintegration of tubercle bacilli lodged in existing lesions, a more reasonable explanation must be sought.

Clinical experience with a number of therapeutic agents in tuberculosis has shown that many of them have in common the property of exerting a nonspecific effect analogous to that of tuberculin. They seem to stimulate more or less of an inflammatory reaction in and about tuberculous foci, which, if not pushed too far, may be turned to good account in some cases, as, for instance in those already tending towards fibrosis and healing. The agents which may act in this way include non-specific proteins, actinic rays, X Rays and certain chemicals, like hetol. Such effects from the introduction of heavy metals are not infrequently witnessed in the treatment of syphilis complicating tuberculosis. Cummins, who thinks that sanocrysin works like other heavy metals, recalls that von Linden noted similar reactions after the administration of copper compounds to tuberculous subjects.

Petersen and Levinsen (49) and Levinsen, Petersen and Milles (50) in a series of fundamental experiments have found a rational explanation of the action of this class of substance.

All the therapeutic agents of the "reactive class", tuberculin, sodium aurothiosulphate (sanocrysin), hetol, etc., act seemingly in a relatively simple way. They first make the tissues more permeable, and later the tissues become less permeable for a considerable period of time.

"The focal reaction, whether in the form that is obvious clinically or consisting merely of the imperceptible biologic reactions following the injections of minute doses of the agents in question, is a reaction that depends on changes in the permeability of the capillaries about the tuberculous focus".

This conception gives us a logical understanding of all the observed reactions except those attributable to the direct toxic effects of the drug itself. In other words, a certain group of sanocrysin induced symptoms, such as fever, rapid pulse, lassitude and loss of weight, can reasonably be interpreted, at least to some extent, as the constitutional effects of circulating tuberculosis "toxins" and these may be liberated from existing tuberculous lesions by some action of the drug. A non-specific action, resulting in an alteration of capillary permeability about the tuberculous lesions would seem to be wholly sufficient to produce such effects. It does not appear necessary to assume a specific bacteriotropic action, - especially as this is pure assumption, and contrary to all the available evidence.

In the minds of many who have used sanocrysin therapeutically there is evident uncertainty in distinguishing its tuberculin-like effect in the tuberculous organism from its direct toxicity. Moellgaard and his co-workers observed that normal subjects experienced little or no harm from the introduction of the drug, whereas the tuberculous sometimes suffered serious damage. This

difference led them to assume that the liberation of toxins from the tuberculous lesions is practically the sole cause of all undesirable effects. The characteristic reactions with fever, vomiting, diarrhoea, stomatitis, skin eruptions and albuminuria, and even the more serious effects such as myocarditis and pulmonary oedema, were ascribed to this mechanism, which, in effect, was assumed to be the same as that operating in serum sickness.

While a tuberculin-like effect enters into the picture and is readily explainable, as discussed above, it seems to be straining the point too far, to accept this as the cause of all the trouble. It is true that an overdose of tuberculin may cause profound constitutional effects but, viewed broadly, these are seldom of the character of certain sanocrysin reactions, which are to be interpreted rather as signs of metallic poisoning. Skin eruptions of the kind or intensity which occur in sanocrysin treatment and stomatitis are never seen from overdosage with tuberculin. Gastrointestinal upsets with loss of weight are not uncommon, but unlike sanocrysin effects, these are not usually so severe as to result in acidosis, nor do they persist long after the febrile reaction to tuberculin has passed.

While in most cases under treatment with sanocrysin, the skin eruptions, stomatitis, and gastrointestinal symptoms develop simultaneously with or following the appearance of fever, it seems significant that in some

cases the rash comes first, whilst in others there may be no raised temperature even though these other manifestations may be severe. If such a syndrome could be assumed to result entirely from the tuberculin-like effect of sanocrysin, one would certainly expect the fever would be much higher and that it would not be antedated by a skin eruption. On this assumption the syndrome is an incongruity, and a more plausible explanation is that the gastrointestinal effects, stomatitis and skin eruptions are caused chiefly if not entirely by the metallic salt itself.

Despite these criticisms of Moellgaard's work, the following statement drawn from his experiments has not yet been disproved, viz., that "certain animals inoculated with a known tubercle strain, which acts fatally on control-animals, can be restored to permanent health if sanocrysin is injected into them intravenously in a certain dosage, given at the right time."

Is there then, a clinical effect corresponding to the practical experimental effect?

As pointed out by Gravensen (51), to give sanocrysin an honest trial, cases must be chosen which are in a condition, as nearly as possible, in agreement with that of recently infected animals. The cases primarily selected must be those who come for treatment at an early stage, during the development of the fresh spreading disease, with exudative infiltrations or disseminated nodules or

both combined. Working on these lines Gravensen treated twenty-six cases and found that they responded well to sanocrysin, improving greatly clinically, with a similar improvement in physical signs and X Ray picture. In all twenty-six cases there was a complete disappearance of any X Ray indication of active fresh disease. Synchronously tubercle bacilli disappeared from the sputum in all cases where it had previously been isolated.

Gravensen concludes that these results approach as nearly as possible to a proof that the clinical effect of sanocrysin of whatever nature it may be, corresponds to that of Moellgaard's experimental work. He extended his line of treatment to cases where fresh and later changes appeared in the same patient. He concludes that in them also the clinical effect answers the experimental in the sense that it is on the fresh spreading disease that the sanocrysin acts specifically, and in the mixed cases this fresh spreading disease could be treated although no appreciable effect could be expected in old fibrous and destructive changes.

His principles of treatment are as follows:-

- (1) Sanocrysin is used primarily when the fresh spreading disease predominates. If there are further changes in the form of cavities, collapse therapy is indicated secondarily.
- (2) Collapse treatment is used primarily when the later changes predominate. Sanocrysin is used as a backing up for the arrest of the fresh spreading disease in the

collapsed lung, and for a fresh extension of the disease in the other lung.

(3) Sanocrysin and collapse treatment are used synchronously when it is evident that sanocrysin at its best will lead to a process of breaking down (with massive infiltration and caseous pneumonia), or where the phase of the disease indicates one kind of treatment for the one lung and different treatment for the other lung.

Brock (52) following the same line of argument in America, tried the drug on the almost purely exudative type of lesion, seen not infrequently in the negro. He obtained disappointing results in his negro cases in comparison with the same type of disease in the white race where he describes his results as "remarkable". This writer suggests that Gravensen's view must be modified. The actual acuteness of the lesion does not appear to be the chief requisite in selecting cases, but a certain amount of immunity must also be present.

The value of sanocrysin in association with collapse therapy is also emphasised by Bernard (53) who gives his indications for its use as follows:-

- (1) Unilateral cases already treated with artificial pneumothorax but in whom there is a recurrence in which a second artificial pneumothorax does not work.
- (2) Artificial pneumothorax not completely efficacious in cases with large X Ray opacities.
- (3) Artificial pneumothorax successful, but spread of disease to the opposite side occurring.

- (4) Bilateral disease from the beginning, artificial pneumo-thorax being induced on the worse side, the drug being given to control the contralateral lung.
- (5) Bilateral disease of a severe type, gold being given in addition to bilateral pneumothorax treatment.
- (6) In place of artificial pneumothorax when this has proved impossible or has been refused.

He states that 50% of his gold treated cases have given favourable results.

Some of the toxic symptoms following the administration of sanocrysin have already been referred to, and may be summarised here. Burrell (54) sets them out as follows:-

1. Febrile reactions. These may be divided into three groups:-

(a) A sudden rise of temperature, starting generally within an hour of the injection, and lasting several hours. There is always a feeling of malaise during the reaction, and sometimes a rigor.

(b) A rise of temperature which may start equally suddenly, but which may persist for a few days, is more severe than the first type of reaction and is accompanied by malaise, headache, and sometimes vomiting.

(c) A long febrile reaction which does not begin until after the third injection of sanocrysin. The rise is gradual and lasts five days or more. It is always accompanied by albuminuria of a slight degree, but with little or no malaise.

2. Albuminuria.

A very faint trace of albumin is found fairly commonly. There is a greater tendency for albuminuria to occur as treatment continues, and this may persist. Clarke (55) states that this occurred in all his treated cases numbering eighteen. He states that no red blood cells nor casts were found in any case. Amberson, McMahon and Pinner (48) found that following the third and fourth injections of sanocrysin all treated cases showed some evidence of renal damage. In the majority of patients this consisted in the appearance of a few red cells, occasional renal epithelial cells and a few granular casts. Some of their patients showed traces of albumin. This, however, was much less regular than the microscopical changes, and was always preceded by the appearance of cellular elements. They consider that a certain amount of renal damage takes place in all patients receiving sanocrysin.

3. Gastrointestinal symptoms.

Vomiting may occur directly after injection, and may be associated with a febrile reaction.

Looseness of the bowels is not uncommon, and may develop into a troublesome diarrhoea.

Stomatitis and a metallic taste in the mouth may also occur.

4. Aching of the limbs and rheumatic pains in the joints.

5. Skin rashes.

These usually take the form of erythematous rashes but may vary from a few small erythematous patches to maculopapular (scarlatiniform and morbilliform) eruptions dis-

tributed over the whole body. Severe cases may go on to a desquamative dermatitis.

Hansburg (56) has described so called "chrysiasis". This consists of a characteristic slate-grey discoloration of the skin in patches where it is exposed to the light - that is, chiefly the hands and face - a discoloration resembling argyria and due to the precipitation of gold in the skin. The precipitation is permanent and of grave importance to the patient. Reddish blonde persons are said to be particularly liable.

Conjunctival injection and neuritis have been described (48). Amberson, McMahon and Pinner (48) also describe one patient who developed jaundice under treatment. This case ended fatally and was ascribed to metallic poisoning by the authors.

A considerable number of cases of agranulocytic angina have also been described as following sanocrysin therapy (57 to 74).

Herpes labialis is an occasional symptom.

The changes in the blood during sanocrysin therapy have been studied by Houghton (76). The author considers that in a general way the differential count indicates potential resistance to the disease, and the sedimentation rate and von Bonsdorff count indicate the condition of the patient as the result of the disease. It was found that roughly patients undergoing treatment fell into two groups according to their immediate reaction to an initial dose of sanocrysin (0.1 or 0.25 gm.)

	<u>Group A.</u>	<u>Group B.</u>
Total leucocytes	Increased	Decreased
Total lymphocytes	Increased	Decreased
Total monocytes	Decreased or slightly decr'd.	Greatly increased.
Sedimentation rate	Decreased	Increased

Cases which ultimately did well tended to fall into Group A., whereas these which failed to improve constantly fell into Group B. There was evidence that a sufficient period of time was not ordinarily allowed to elapse between doses, and his results showed that the influence of an injection is still evident after fourteen days. Equally marked changes in the haemogram were produced by doses of 0.1 gm. as by doses of 0.5 gm.

The sedimentation rate showed in certain cases an immediate but temporary improvement after an injection, this being regarded as a good response. The sedimentation rate tended to improve with the rest of the haemogram in all satisfactory cases. Heaf (77) also found this of value in assessing the prognosis of sanocrysin treated patients. Houghton also states that sanocrysin rashes were always accompanied and in some cases preceded by an eosinophilia. On the evidence of the blood changes, small doses (0.1 gm.) were found as efficacious as larger doses (0.5 gm.) and the writer states his belief that better results can be obtained by extending the interval between doses to fourteen days.

The question of dosage is one upon which divergent views are still held.

Secker (78) holds that many of the poor results reported are due to faulty - usually too low- dosage. All animal experiments have shown the desirability of giving from 1.5 to 2.0 cgm. per kilo. of body weight. His usual dosage in patients has been 0.5, 0.75, 1.0 gm., the last dose being repeated or increased to 1.25 or 1.5 gm. if the weight of the patient warranted it. His first two or three doses are given at two-day intervals and the others at intervals of four, five or six days. Patients with acute pneumonic processes have only 0.25 or 0.35 gm. at the first injection as they are likely to have severe intoxication. If practicable the treatment is continued until there is no reaction after doses of 1.5 or 2 cgm. per kilo. of body weight, and is then followed by a sanatorium regime. Secker is convinced that better results are obtained by giving large doses which cause reactions than small doses which do not cause reactions. The latter method requires a large number of injections, of which the early ones are quite useless therapeutically and only increase the amount of metal stored in the organism. The absence of a reaction is considered by Secker to be by no means a desideratum; the activation of a focus, especially an old focus, may be of the greatest importance to later healing.

Pask (79) on the other hand states that the dosage should be regulated by the reaction of the patient. In an undersized person with poor resistance and unsteady

temperature his initial doses is very small - 0.025 gm. and in the average case 0.05 gm. In the absence of reactions the dose is gradually increased to 0.75 gm. the total amount given being 5 to 6.5 gm. The smaller doses are given at intervals of four to five days, and larger doses at intervals of seven to ten days. An uneventful course takes twelve to fifteen weeks, but some of his cases take much longer. He keeps his patients in bed for twenty-four hours after each injection.

Fabri (80) advocates small doses such as those of Pask, rising gradually to a maximum of 0.5 gm.

Mayer (81) treats over 300 patients weekly in Paris with gold, most of whom attend the Laennec Hospital as out-patients. He varies his technique and dosage according to the state of the patient and the initial result of the treatment. In apyrexial cases, after a preliminary injection of 0.1 and a week later of 0.15 gm. of "Crisalbin" in 5 cc. of distilled water, he gives weekly injections of 0.25 gm. for four months. If there have been no reactions and the patient is improving, the injections are continued for another period of four months, when the dosage is again reconsidered. If there have been reactions, he continues the weekly injections, but as a solvent substitutes 10 cc. of a 10% solution of calcium gluconate, for 5 cc. of distilled water. If after four months the patient has not improved or the disease has spread, though without reactions, he increases the dose to

0.5 gm. using 10 cc. of the calcium gluconate solution. If after four months of this dosage there is still no improvement he abandons the treatment. In febrile cases he uses calcium gluconate as a solvent and advocates 0.25 gm. crisalbin for six weeks, and then 0.5 gm. for six weeks, and then 0.75 or even 1 gm. if there has been no improvement. He continues treatment for many months, but when the sputum becomes free of tubercle, the intervals between doses may be increased to a fortnight. He summarizes his results of 404 cases who have been under treatment for not less than six months as one third not influenced, one third improved, and one third much improved or cured.

Wurtzen and Sjørslev (82) treated 145 cases with small doses and found improvement in 68%.

Faber (83) compared the results of large and small dosage in two groups of cases and obtained better results with the latter.

Mansell (84) after a trial of dosage based on the principles of Secker, gave this up and now advocates only small doses.

The general consensus of opinion among present day clinicians appears to be that large doses are dangerous and that better results are to be obtained by small doses carefully judged according to the clinical condition and tolerance of the individual patients.

The present day opinion as regards sanocrysin therapy may be briefly summed up as follows:-

- (1) Most authors agree that sanocrysin is of value (85): some French workers (86) consider that the results do not justify the risk.
 - (2) Complications appear to be definitely more frequent and more severe with large doses than with smaller.
 - (3) The exudative type, provided it is not too acute or too extensive gives the most successful results, although the Japanese specially favour the proliferative type (87).
 - (4) Very advanced cases or those with poor resistance are made worse.
 - (5) Chronic fibroid cases show temporary benefit but acute exacerbations of chronic disease respond favourably.
 - (6) The most constant results are the diminution in amount of sputum and its bacillary content; the majority of cases appear to become sputum positive again, however. Changes in the physical signs are less constant.
 - (7) X Ray improvement has been noted by many workers.
 - (8) Roughly 50% of all cases have shown some degree of improvement.
 - (9) Sanocrysin is shown to great advantage as an adjuvant to artificial pneumothorax both for the collapsed and for the contralateral lung.
 - (10) The results of collapse therapy are far superior to those of sanocrysin, in virulent disease, but sanocrysin may make an artificial pneumothorax possible in bilateral disease, where otherwise it would be precluded by the nature and extent of the contralateral disease.
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S U M M A R Y

of 24 Cases of Pulmonary Tuberculosis

Treated by Gold Therapy.

The following twenty-four cases were all admitted to Holly Lane Sanatorium, Smethwick, during the year 1934. They had all been seen and examined previously, either at the tuberculosis dispensary or at their homes.

Holly Lane Sanatorium admits only early or relatively early cases and a large proportion of the patients admitted have some form of collapse therapy, this being utilised as widely as possible. Gold treatment has been used during the past two years but only where collapse therapy could not be instituted, or in association with collapse therapy under special circumstances, such as spread of the disease to the uncollapsed lung. Thus the first seven cases were all treated primarily by artificial pneumothorax, but all had either at the commencement of treatment or at a later date some spread of disease to the contralateral lung.

Cases chosen apart from this group were, as far as possible, those who came for treatment at a relatively early stage during the development of the fresh spreading disease with exudative infiltrations or disseminated nodules or both combined. This is the class of case which Gravensen (93) and others have shown to be the most suitable for this form of treatment, and which conforms most closely with Moellgaard's experimental work (15).

Cases 8 to 20 form this group in the present series. In selecting this group, the greatest care was taken to include only cases of such extent of the disease that there was no possible doubt as to the diagnosis and in fact, all these cases, with only one exception, had positive sputa. The one exception (Case 16) never had any sputum whilst under observation, but the other findings left no doubt as to the diagnosis. No case was rejected on account of great extent, other conditions being suitable.

The third and last group, comprising cases 21 to 24 were more chronic in nature, with fibrous lesions predominating, but each of these cases had had a recent spread of the disease and it was here, more an attempt to check an exacerbation in the course of a chronic disease rather than an effort to obtain a "cure".

The dosage chosen has been that of small, frequently repeated doses regulated by the size and clinical condition of the patient as advocated by Pask (79), and the procedure has been based largely on the work of Mayer (81).

The salt used has been "Crisalbin" and the initial dose in each case 0.025 gm. dissolved in 5 c.c. of distilled water, intravenously. This dose was increased

to 0.05 gm., 0.1 gm., 0.15 gm., and ultimately to 0.25 gm., in the first course, if there were no reactions, doses being given at three day intervals. A total of from 5 to 6 gm., was aimed at for one course, this usually taking about fourteen weeks. If any reactions ensued a rest from treatment was given, and when treatment was recommenced 10 c.c. of Calcium Gluconate was substituted for 5 c.c. of distilled water. In all febrile cases also, Calcium Gluconate was used as the solvent.

If after the first course the patient had not improved, or the disease had spread, though without reactions, the dose in the second course, which was begun after a rest of about two months, was increased to 0.5 gm, 0.75, or even 1.0 gm.

During their first course at least, all patients were completely at rest in bed. During subsequent courses they might be ambulant in the sanatorium if their condition warranted it, or after discharge, attending as out patients at the tuberculosis dispensary.

On admission, in addition to a clinical and radiological examination, all patients had a white blood count, a differential count, and a red cell sedimentation rate test, performed. The urine was examined chemically and microscopically and this was repeated weekly in all cases undergoing gold treatment.

Blood counts and sedimentation rates were performed monthly. Radiograms were repeated regularly at several months interval throughout treatment, or more frequently if thought necessary.

The sputum was examined on admission, and all positive cases were repeated monthly. Where a sputum was negative to commence with or became negative during the course of treatment, microscopical examinations were repeated thrice weekly. Every patient's sputum was measured twice weekly.

Blood sedimentation rate tests were made according to the technique described by Westergren (105), the fall in millimetres being read at the end of the first hour.

When attending as out patients at the dispensary, the urine was examined as above at weekly intervals in addition to the usual temperature, pulse rate and clinical records. Sputum tests were performed monthly.

All these patients have now been under close observation in sanatorium and at the tuberculosis dispensary throughout a period of two years, so it is felt that a good indication of the value of the treatment in these cases may now be had from a study of the results to date.

CASE No. 1.

Male, aged 22 years. Admitted 7. 6. 34.

History: Two attacks of right sided pleurisy since December of previous year. Lassitude for several months, and recently a cough and sputum.

Physical signs: Dullness over right upper lobe with bronchial breathing below the clavicle and post tussic crepitations. Some dullness at left apex with a few fine crackles.

X-Ray: Infiltration at right upper lobe with cavity formation; adhesions at right base to diaphragm; increase in striae with mottling in left upper lobe.

General condition poor. Weight 8 st. 13 lbs.

Sputum - positive. Temperature 98.2°- 99°F.

Sedimentation Rate	17.
Polymorphs	69%
Lymphocytes	25%
Mononuclears	4%
Eosinophils	2%

An artificial pneumothorax was attempted on 21. 6. 34. and a collapse of the upper lobe obtained. A phrenicectomy was performed on 2. 8. 34, and a much better collapse of the whole lung obtained.

Crisalbin was commenced on 17. 8. 34. Dosage: 0.025 gm. 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued until 27. 11. 34. Total 6.275 gm.

Patient's weight had now increased to 9 st. 7 lbs., and the sputum was negative. Temperature was normal and the patient was feeling extremely well.

Discharged 22. 12. 34.

Weight 9 st. 9 lbs. A good collapse of the right lung was present, and no moisture was now audible at left apex. Slight cough but no sputum.

Sedimentation Rate	6.
Polymorphs	68%
Lymphocytes	28%
Mononuclears	3%
Eosinophils	1%

CASE No. 1. (Cont.)

A second course of Crisalbin from 2. 2. 35. to 18. 5. 35. was given with dosage similar to course one, total 6.275 gm.

Weight now 9 st. 13 lbs., no cough or sputum. Work as a "lorryman's mate" was commenced on 23. 5. 35. and the patient has been working since.

On 20. 6. 36. the weight had increased to 10 st. 10 lbs. Artificial pneumothorax treatment was still being carried out on the right side and there was no clinical evidence of any active disease of the left side. No cough and no sputum. The X-Ray showed some fibrosis at the left apex but otherwise no evidence of active disease in the left lung.



16. 8. 34.



20. 6. 36.

CASE No. 2.

Female, aged 17 years.

History of tubercular axillary glands on left side at age of twelve; treated conservatively. For two months, lassitude and loss of weight; cough for two days, no sputum.

Physical signs: Slight impairment of percussion over middle lobe; breath sounds vesicular, no accompaniments.

X-Ray: Fine tubercular mottling throughout middle lobe.

Admitted 17. 7. 34. Weight 6 st. 8 lbs. General condition poor. Temperature 100.5°F. evenings, 98°F. mornings.

Sedimentation Rate	56.
Polymorphs	74%
Lymphocytes	16%
Mononuclears	10%
Eosinophils	0%

Crisalbin started 6. 8. 34. Dosage: 0.025 gm. 0.025, 0.025, 0.05, 0.05, 0.1, 0.1, 0.1, 0.15, 0.15, gm. at three day intervals.

The temperature continued to swing to 100.5° to 101°F. in the evenings and it was thought better not to give a larger dose than 0.15 gm. This was therefore continued at three day intervals. Artificial pneumothorax induced 11. 10. 34. Following this, the temperature showed some signs of improvement for about a month, but then again rose to its previous level. Sputum was now present and on 16. 11. 34. was found to contain tubercle bacilli.

Improvement began to take place during January 1935. and by the end of February 1935. the temperature was normal night and morning, whilst at rest in bed. Sedimentation rate still 42. Total Crisalbin to 27. 2. 35. 6.3 gms.

Temperature rose again on patient being allowed up for one hour so that complete rest was once more reverted to. Temperature continued to show an evening elevation to 100.5° during March and April, 1935. Sedimentation rate 26. 4. 35. - 52. Sputum positive.

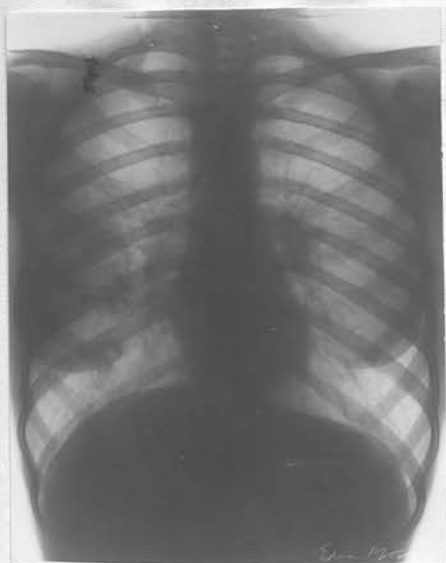
CASE No. 2 (Cont.)

Second course of Crisalbin started 2. 5. 35. Dosage: 0.1, 0.1, 0.15 gm. This latter dose was continued at three day intervals. Temperature continued to swing, and the patient's general condition got steadily worse.

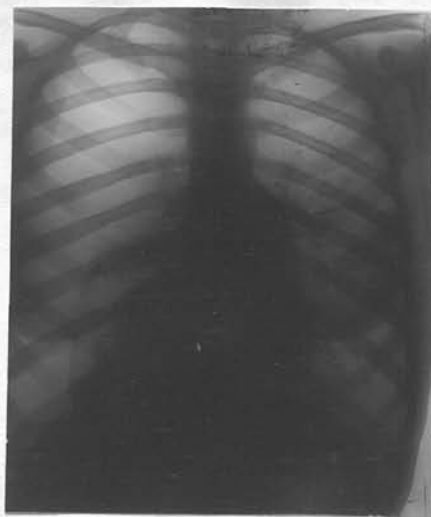
X-Ray on 7. 7. 35. showed spread of the disease to the left upper lobe.

Crisalbin stopped 4. 8. 35. Total of second course 3.0 gm.

Condition grew steadily worse, the disease showing steady progression in the left lung. Artificial pneumothorax was stopped on 10. 8. 35. this making no difference to the local or systemic symptoms. Both lungs showed fresh foci of infections, and the patient passed into a state of severe cachexia and died on 17. 11. 35.



20. 7. 34.



7. 7. 35.

CASE NO. 3

Female, aged 25 years. Admitted 4. 2. 34.

History of "influenza" two months previously which had left her feeling tired and 'run down.' Had been troubled with a cough since the attack and lately had been bringing up sputum; had noticed herself getting thinner.

Physical signs: Impairment of percussion note over right upper lobe below clavicle; breath sounds bronchial, no accompaniments.

X-Ray: Subclavicular type of infiltration right upper lobe.

General condition poor, weight 7 st. 10 lbs.

Sputum - positive. Temperature 98° - 99.2°F.

Sedimentation Rate	16.
Polymorphs	74%
Lymphocytes	22%
Mononuclears	3%
Eosinophils	1%

Artificial pneumothorax induced on right side 10. 2. 34. and a good collapse obtained. The patient's general condition improved steadily. Her sputum after a month disappeared altogether and after three months her cough also ceased. By 20. 6. 34. she had gained 6 lbs. and was up for six hours each day. Her cough again returned, however, and in addition her temperature commenced to rise again. Her sputum which had ceased, returned, and contained tubercle bacilli.

X-Ray on 2. 7. 34. showed the presence of a new focus in the left upper lobe.

She was put back to bed, and Crisalbin started on 6. 7. 34. Dosage: 0.025 gm, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 23. 10. 34. Total 6.25 gm.

The sputum had become negative on 2. 9. 34. and ceased altogether 16. 10. 34. The patient's general condition was now very good, weight 8 st. 2 lbs; no cough, no sputum.

CASE No. 3 (Cont.)

Sedimentation Rate	8.
Polymorphs	72%
Lymphocytes	25%
Mononuclears	2%
Eosinophils	1%

No abnormal physical signs could be made out over the left lung, but the X-Ray picture was unchanged.

The patient was discharged on 18. 12. 34. feeling very well indeed. Weight 8 st. 5 lbs.

Second course of Crisalbin started 4. 3. 35. Dosage: 0.025 gm, 0.05, 0.1, 0.1, 0.15, 0.25 gm. twice weekly. 0.25 gm. was continued until 28. 6. 35. Total 5. 75 gm.

The patient was then still 8 st. 5 lbs., and feeling very well, no cough or sputum. X-Ray picture still showed a good collapse of the right lung and some improvement in the left lung.

A third course similar to the second lasted from 4. 10. 35. to 27. 1. 36.

The patient was then feeling so well that leave to work as a "sorter" was given. Since then she has continued to work regularly and has been symptomless. The right lung was allowed to re-expand during April and May 1936.

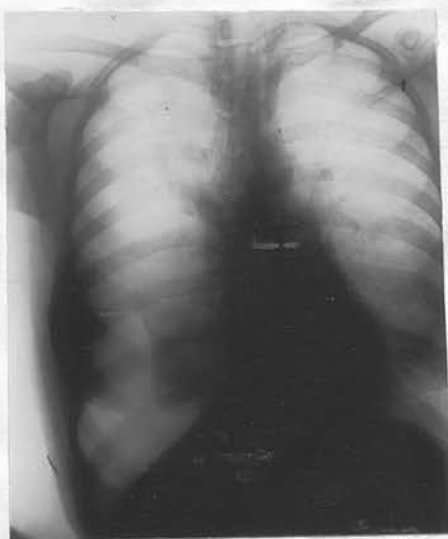
On 4. 6. 36. patient was 8 st. 6 lbs, no cough or sputum and feeling well.

X-Ray showed an increased fibrous tissue in the right upper lobe, no cavity and no evidence of disease in this area; the left apex showed some increase in the normal lung striae, but no evidence of active disease.

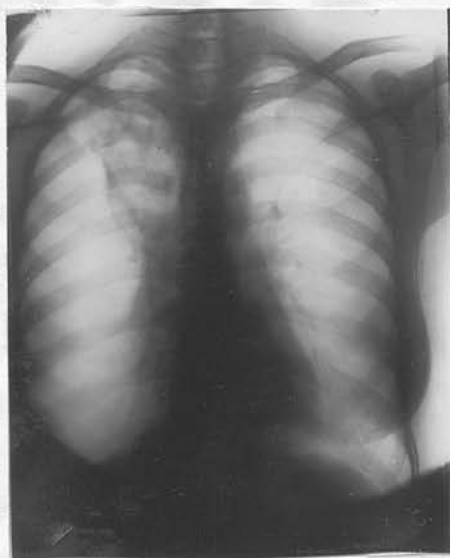
CASE 3.



6. 2. 34.



2. 7. 34.



24. 4. 36.

CASE No. 4.

Female, aged 19 years. Admitted 17. 9. 34.

History of febrile illness five weeks before, with cough which had persisted, lassitude and loss of weight.

Physical signs: Impairment over left upper lobe with a few post tussic crepitations, breath sounds vesicular. Slight impairment above right clavicle.

X-Ray: Tubercular infiltration left upper lobe with early cavity formation; some increase in striae at right upper lobe with stippling.

General condition fairly good. Weight 7 st. $3\frac{1}{2}$ lbs.

Sputum - very scanty; tubercle bacilli present.

Sedimentation Rate	18.
Polymorphs	72%
Lymphocytes	21%
Mononuclears	7%
Eosinophils	0%

An artificial pneumothorax was induced on the left side on 18. 9. 34. and a good collapse obtained. A month after the induction, a course of Crisalbin was commenced in order to control the disease on the right side. Dosage: 0.025 gm, 0.05, 0.05, 0.1, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 12. 1. 35, a total 6.1 gm. having been given. No reactions were experienced and the patient's condition improved steadily. Her weight had increased to 7 st. 8 lbs., and she had lost her cough and sputum. She began to be allowed out of bed at this time and after six weeks interval, another course of Crisalbin similar to the first was given, commencing on 22. 2. 35., and finishing on 4. 5. 35, a total of 6.1 gm. again being given. The patient was now up all day; her weight had increased to 8 st. 1 lb. and she no longer suffered from lassitude, cough or sputum.

Sedimentation Rate	7.
Polymorphs	67%
Lymphocytes	29%
Mononuclears	4%
Eosinophils	0%

CASE No. 4 (Cont.)

Physical signs: Nothing abnormal on right side.

X-Ray: Good collapse of left lung, some increase in striae at right apex, no stippling present.

Patient was discharged on 17. 5. 35. and the following month was sent to Davos where she has remained since. A report on 19. 6. 36. states that her condition is excellent, weight 8 st. 9 lbs, quite free from symptoms, and nothing abnormal to be found at the right apex clinically or radiologically. Artificial pneumothorax still maintained on left side.

CASE No. 5.

Female, aged 24 years. Admitted 8. 6. 34.

History of cough and loss of weight for four months; lassitude marked.

Physical signs: Dullness and crepitations over left apical region; bronchial breathing below clavicle.

X-Ray: Subclavicular infiltration left upper lobe with cavity formation; right lung clear.

General condition poor. Weight 7 st. 5½ lbs.

Temperature 98°- 99.2°F.

Sedimentation Rate	34.
Polymorphs	73%
Lymphocytes	17%
Mononuclears	10%
Eosinophils	0%

Sputum - positive.

An artificial pneumothorax was induced on the left side on 22. 6. 34. and a good collapse obtained. The patient's general condition improved somewhat following this, the temperature tending to settle and weight being put on steadily. On 26. 7. 34. however, she had a sudden rise of temperature to 103.2°F. which fell gradually during the next five days. This was associated with malaise and headache. Following this, the temperature varied between 98° and 99.4°F. and a few post tussic crackles were heard at the right apex. An X-Ray picture revealed the presence of a new focus in the upper lobe of the right lung and on 28. 8. 34. a large annular shadow was present. Pneumothorax treatment was continued and a course of Crisalbin was commenced on 4. 9. 34. Dosage: 0.025 gm. 0.025, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.025 gm. was then continued twice weekly until 18. 12. 34. a total of 5.85 gm. being given.

The general condition had improved considerably, the weight being now 8 st. 12½ lbs. The temperature was settled but cough still persisted and the sputum still contained tubercle bacilli. The sedimentation rate was still 32, and an X-Ray picture showed new exudative lesions spreading in the right lung.

CASE No. 5 (Cont.)

The patient was kept at complete rest and a second course of Crisalbin was started on 1. 2. 35. Dosage: 0.025 gm. 0.05, 0.1, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly for four weeks and then the dose was increased to 0.5 gm. once weekly for three weeks and subsequently 1.0 gm. weekly for two doses. Total 6.275 gm; course completed on 3.5. 35.

There were no reactions and the patient's general condition continued good. Weight was now 9 st. 1 lb., temperature normal, but an X-Ray showed still further spread in the right lung and also in the collapsed lung.

Sedimentation Rate	38.
Polymorphs	71%
Lymphocytes	18%
Mononuclears	11%
Eosinophils	0%

Because of the obvious spread in the centre lateral lung, the artificial pneumothorax was abandoned. This did not affect the temperature in any way. This patient showed very little systemic reaction to spreading exudative disease and obviously very little resistance.

Discharged on 17. 5. 35.

After two months at home and ambulant, her weight had fallen to 8 st. 6 lbs. and lassitude was marked. Cough was troublesome and sputum positive.

A third course of Crisalbin was started on 24. 7. 35. and carried on until 2. 11. 35. Dosage was similar to course two, a total of 6.275 gm. being given.

The weight had now fallen to 8 st. 1 lb. and the sputum was still positive.

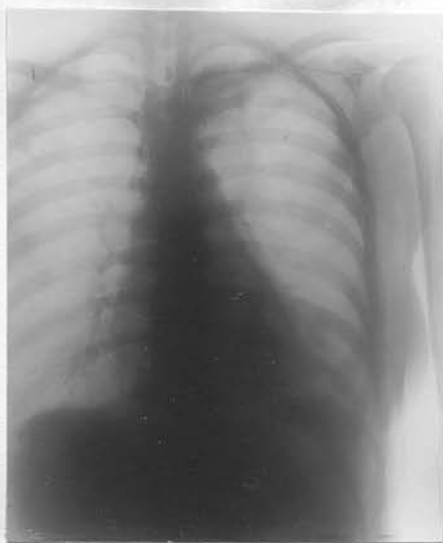
An attack of pleurisy supervened on 4. 1. 36. which kept the patient in bed for five weeks with a temperature of 99.6°F.

Since then she has steadily lost ground and on 22. 5. 36. her weight was only 7 st. 8 lbs. No further

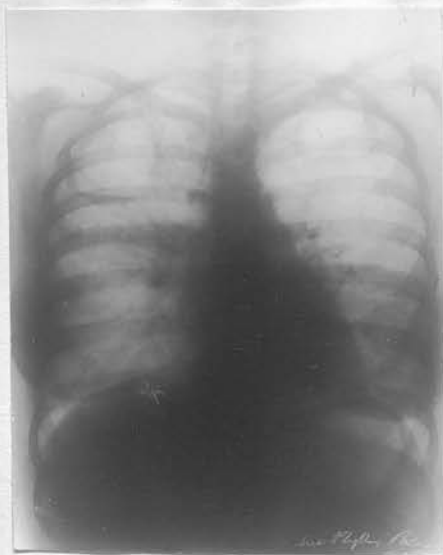
CASE No. 5. (Cont.)

gold has been given as the patient showed absolutely no benefit from its administration, but the disease continued to spread.

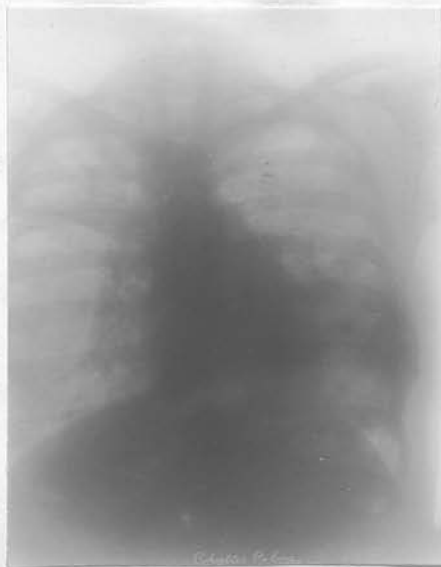
A further X-Ray on 22. 5. 36. showed considerable extensions in both lungs.



28. 7. 34.



28. 8. 34.



22. 5. 36.

CASE No. 6.

Female, aged 17 years. History of six months languor and loss of weight; cough for two months.

Physical signs: Impairment of percussion note in right apical region above and below clavicle; breath sounds bronchial in this area, and a few post tussic crepitations heard posteriorly in supra-scapular region.

X-Ray: Subclavicular type of infiltration right upper lobe. Left lung clear.

Admitted 14. 5. 34. Weight 6 st. $3\frac{1}{2}$ lbs. Temperature 99° F. in the evenings. Sputum - positive.

Sedimentation Rate	32.
Polymorphs	66%
Lymphocytes	22%
Mononuclears	12%
Eosinophils	0%

Artificial pneumothorax induced on right side 2. 6. 34 and good collapse attained. Progress satisfactory during next two months. Temperature then again rose and the sedimentation rate which had fallen to 12, rose again to 28. X-Ray showed the presence of an early infiltration in the middle zone of the left lung.

Course of Crisalbin commenced 13. 8. 34. Artificial pneumothorax continued.

Dosage: 0.025 gm, 0.05 gm, 0.05 gm, 0.1 gm, 0.1 gm, 0.15 gm, 0.15 gm, 0.25 gm. at three day intervals. Subsequently, doses of 0.25 gm. were continued at three day intervals.

Discharged 4. 2. 35. Total Crisalbin 6.25 gm.

Condition on Discharge: Weight 7 st. 2 lbs. Afebrile.

X-Ray: Good collapse of right lung; infiltration in left lung of less extent than on 8. 8. 34.

Sedimentation Rate	10.
Polymorphs	55%
Lymphocytes	36%
Mononuclears	6%
Eosinophils	3%

CASE No. 6 (Cont.)

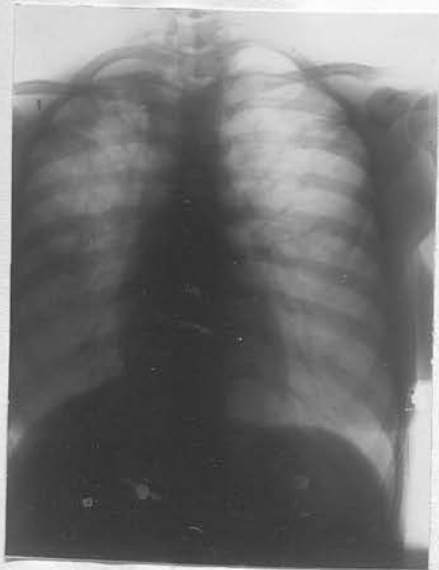
Subsequent progress: Second course of Crisalbin commenced 8. 5. 35. 5.75 gms. given; dosage 0.25 gm. twice weekly; finished 14. 9. 35.

Third course commenced 16. 1. 36. 6.0 gms. given; similar dosage to second course; finished 10. 5. 36.

During April and May the artificial pneumothorax was allowed to re-expand.

X-Ray 16. 5. 36. Fibrosis at right apex, and some increase in striae in middle zone of left lung, but no radiological evidence of active tubercular disease.

Weight 16. 5. 36. 8 st. 1 lb. General condition excellent. No cough or sputum. Doing housework regularly with no fatigue. No clinical evidence of any active disease in left lung.



11. 5. 34.



16. 5. 36.



CASE No. 7.

Female, aged 15 years. Admitted 4. 11. 34.

History - "pneumonia" six weeks ago which had left patient with a cough, considerable loss of weight and sweating at night; lassitude marked.

Physical signs: Signs of consolidation of middle lobe with marked bronchial breathing; impairment over left upper lobe with showers of fine crackles.

X-Ray: Dense homogenous shadow throughout middle lobe, marked mottling of both upper lobes.

Sputum - scanty. Tubercle bacilli present.

General condition very poor. Weight 6 st. $\frac{1}{4}$ lb.

Sedimentation Rate	32.
Polymorphs	70%
Lymphocytes	15%
Mononuclears	14%
Eosinophils	1%

Temperature 98°F - 102.6°F.

Complete rest in bed was maintained during the first two months and no active treatment was adopted, the temperature continued to swing between 98 and 102°F. and the general condition remained very poor.

An artificial pneumothorax was then induced on the right side on 7. 1. 35. A complete collapse of the lower lobe was obtained with an upward swing towards the middle and collapse of the upper lobe. Following this the temperature tended to settle more and the general condition improved somewhat. A month later (10. 2. 35) small doses of Crisalbin were commenced. Dosage: 0.025 gm, 0.025, 0.05, 0.05, 0.1, 0.15 gm. at three day intervals; 0.15 gm. was continued twice weekly during the next two months and then 0.25 gm. was given for four weeks, finishing 1. 5. 35; total 4.9 gms. The general condition was now very definitely better; weight had increased to 6 st. $6\frac{1}{2}$ lbs, and the patient had lost her sputum, although there was still a morning cough. The temperature was normal, and she felt "better than she had for months".

CASE No. 7 (Cont.)

She was now allowed up for a short time, and a second course of Crisalbin was started on 2. 7. 35. Dosage: 0.025 gm. mounting gradually at three day intervals to 0.25 gm. which was continued to 19. 10. 35, a total of 5.15 gm. being given. Patient was now up for six hours; her weight had increased to 6 st. 11 lbs, temperature normal, no sputum. Sedimentation rate had now fallen to 14.

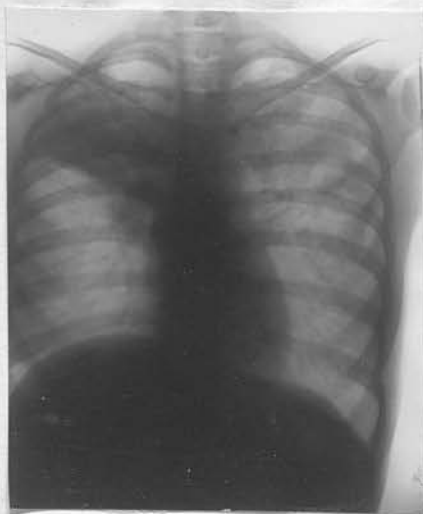
A third course of Crisalbin similar to the second was started on 2. 1. 36, a total of 5.15 gm. again being given; this was completed on 10. 4. 36.

Patient was now up all day and feeling very well. She had still some morning cough, but no sputum. Weight had increased to 7 st. 2 lbs, and sedimentation rate had fallen to 10.

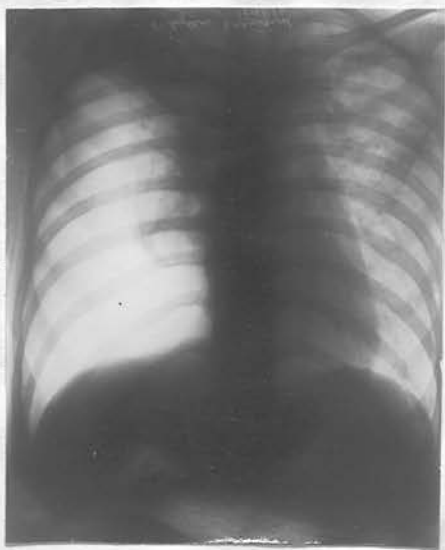
Polymorphs	70%
Lymphocytes	22%
Mononuclears	6%
Eosinophils	2%

Discharged on 19. 4. 36, feeling very well; artificial pneumothorax present on right side, considerable improvement in physical signs and X-Ray picture on left.

Examined again on 17. 6. 36, prior to a further course of Crisalbin. Improvement maintained, weight increased to 7 st. 5 lbs. Further improvement in physical signs on left side.



7. 11. 34.



1. 4. 36.

CASE No. 8.

Female, aged 19 years.

History of loss of weight and languor for three months, cough for about eight weeks and sputum for two weeks.

Physical signs: Impairment of percussion at right apex to upper margin of second rib in front; at left apex impairment above clavicle; area of dullness below angle of right scapula. Breath sounds harsh in right apical region with numerous fine crepitations audible above clavicle; vesicular over whole of left lung with no accompaniments; blowing breath sounds at angle of right scapula.

X-Ray: Mottling at right base with cavity formation; increase in striae at both apices with mottling, more marked on right side.

Sputum: Tubercle bacilli present.

Admitted 8. 5. 34. Weight 7 st. 10 lbs. Temperature 99.5°F. to 100.1°F. in evenings.

Sedimentation Rate	44.
Polymorphs	72%
Lymphocytes	16%
Mononuclears	12%
Eosinophils	0%

Crisalbin started 2. 6. 34. Dosage: 0.025 gm. 0.025, 0.025, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm; this last dose was continued as a maximum dose. All doses given at three day intervals. Total given - 6.5 gm.

Discharged 14. 12. 34.

Condition on Discharge: General condition very good; weight 8 st. 8 $\frac{1}{4}$ lbs. Only slight morning cough; sputum negative.

X-Ray: Condition at right base unchanged; no increase in extent of apical involvements.

Sedimentation Rate	12.
Polymorphs	68%
Lymphocytes	25%
Mononuclears	7%
Eosinophils	0%

CASE No. 8 (Cont.)

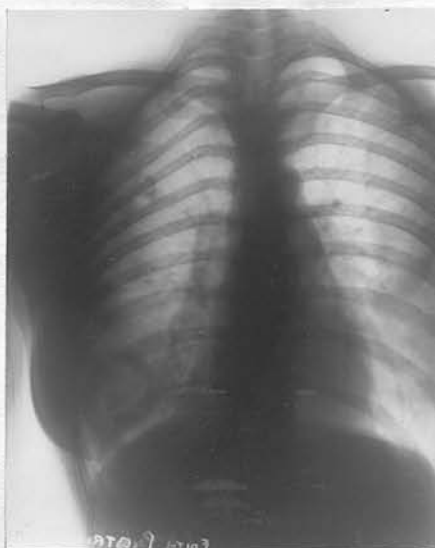
Subsequent progress: Second course of Crisalbin commenced 8. 3. 35. 0.25 gm. given twice weekly; total amount given 5.5 gm.

Third course commenced 10. 11. 35. Dosage and total amount given similar to course two.

Condition on 16. 6. 36: Weight 8 st. 12 lbs. General condition excellent; working as a general housemaid. No cough or sputum, afebrile, and feels extremely well.

Physical signs: Impairment of percussion note in both apical regions, breath sounds vesicular, no accompaniments audible; breath sounds blowing at angle of right scapula.

X-Ray: Increase in striae at both apices, no mottling now visible; cavity present at right base, but considerable clearing of mottling in surrounding lung area.



16. 6. 36.

CASE No. 9.

Male, aged 27 years. Admitted 19. 7. 34.

History of pleurisy two years ago. Cough for about three months, sputum for two months; languor not marked; slight loss of weight recently.

Physical signs: Impairment of percussion over right apex and at right base; post tussic crepitations audible at right apex anteriorly and posteriorly, also at right base.

X-Ray: Increase of striae at both apices with stippling, more marked at right apex; large annular shadow at right base.

Sputum - Positive.

Sedimentation Rate	18.
Polymorphs	64%
Lymphocytes	27%
Mononuclears	7%
Eosinophils	2%

Weight 8 st. 10 lbs. General condition good; slight evening pyrexia.

Course of Crisalbin started 25. 7. 34. Dosage: 0.025 gm, 0.05, 0.1, 0.15, 0.25 gm, at intervals of three days; 0.25 gm. continued at three day intervals until 12. 11. 34. Total Crisalbin 6 gm.

Weight now 9 st. 8 lbs; no accompaniments audible at either apex, but still present at right base. No cough, slight morning sputum, afebrile.

Sputum - Negative.

Sedimentation Rate	8
Polymorphs	66%
Lymphocytes	28%
Mononuclears	4%
Eosinophils	2%

Discharged 16. 11. 34.

Second course of Crisalbin started 22. 2. 35. Patient now working regularly as a mechanic. Weight 9 st. 6 lbs., no cough, slight morning sputum. Sputum negative. Dosage: 0.25 gm. twice weekly; total amount given in second course 6.5 gm.

CASE No. 9 (Cont.)

Condition on 8. 6. 35.

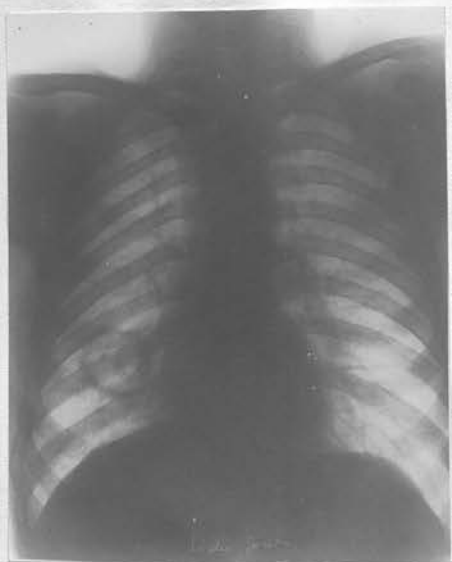
Weight 8 st. 9 lbs. No cough or sputum; working regularly; feeling very well.

Condition on 10. 6. 36.

Has not missed a day's work for eighteen months. No cough or sputum; feels very fit. Weight 9 st. 12 lbs.

X-Ray: Increase in striae at both apices, no stippling now visible; annular shadow still present at right base but very much smaller.

Physical signs: Impairment at right apex and at right base. Breath sounds faint at right base, no accompaniments audible.



12. 7. 34.



10. 6. 36.

CASE No. 10.

Female, aged 23 years. Admitted 23. 8. 34.

History of cough and sputum for six months; lassitude marked; loss of weight.

Physical signs: Impairment of percussion over both upper lobes; bronchial breath sounds below clavicle on each side; numerous moist sounds over upper lobes anteriorly and posteriorly. General condition poor. Weight 7 st. 9½ lbs. Sputum positive. Slight evening pyrexia.

X-Ray: Disseminated foci in both upper lobes, with some increase in fibrosis and early cavitation.

Sedimentation Rate	22.
Polymorphs	68%
Lymphocytes	20%
Mononuclears	10%
Eosinophils	2%

Course of Crisalbin started 23. 8. 34. Dosage: 0.025 gm, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals; 0.25 gm. continued twice weekly until 4. 12. 34. Total Crisalbin given 6.0 gm.

General condition improved steadily. Sputum became negative on 14. 10. 34. and remained negative until discharge.

Discharged 14. 12. 34. General condition much improved; sputum reduced from 3 ozs. to 1 oz. negative; weight 8 st. ¼ lb.

Sedimentation Rate	10.
Polymorphs	70%
Lymphocytes	26%
Mononuclears	3%
Eosinophils	1%

Commenced second course of Crisalbin on 4. 3. 35: finished 16. 6. 35. Weight then 8 st. 3½ lbs, sputum negative. Dosage: 0.25 gm. twice weekly. 6.5 gm. given.

Weight 8 st. 6 lbs; no cough or sputum; feeling very well.

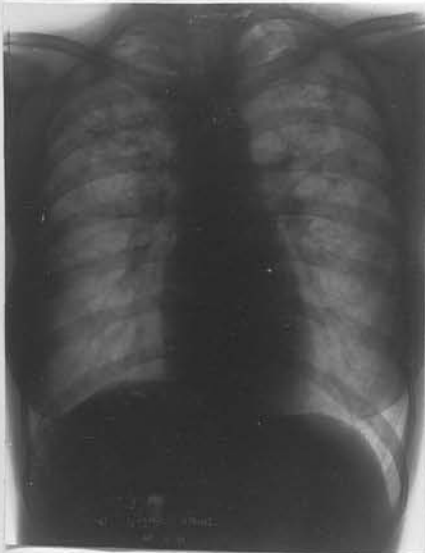
Condition on 24. 6. 36.

Weight 8 st. 8½ lbs. General condition excellent; feeling very well and doing housework regularly; no cough or sputum.

CASE No.10 (Cont.)

Physical signs: Impairment of percussion over both upper lobes, with harsh breath sounds; a few post tussic crepitations over right apex posteriorly.

X-Ray: Marked fibrosis throughout both upper lobes. Considerable radiological improvement.



15. 8. 34.

24. 6. 36.

CASE No. 11.

Male, aged 26 years. Admitted 2. 5. 34.

History of lassitude for three months, with cough and sputum during the past month and a small haemoptysis three days before admission.

Physical signs: Dullness with post tussic crepitations at both apices.

X-Ray: Infiltrations with some fibrosis in both upper lobes.

General condition fairly good. Weight 9 st. 2 lbs.

Sputum - positive. Temperature 98°- 99.2°F.

Sedimentation Rate	18.
Polymorphs	65%
Lymphocytes	28%
Mononuclears	5%
Eosinophils	2%

Crisalbin started 15. 5. 34. Dosage: 0.025 gm. 0.05, 0.1, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued until 28. 8. 34. a total of 6.075 gm. being given.

Patient's weight had increased to 9 st. 12 lbs. Sputum was now negative, and the temperature was normal. He was allowed up, and a second course was commenced on 4. 10. 34. lasting till 18. 12. 34. Dosage similar to course one, total 5.625 gm.

Discharged 22. 12. 34.

Sedimentation Rate	6.
Polymorphs	67%
Lymphocytes	27%
Mononuclears	3%
Eosinophils	3%

Weight 10 st. 4 lbs. No cough or sputum.

He returned to his work as a "packer" in an electrical firm on 4. 2. 35. and has worked regularly since. Another course of Crisalbin similar to courses one and two was given from 2. 4. 35. to 10. 7. 35. Total 6.1 gm.

CASE No. 11 (Cont.)

The physical signs had now improved, no moisture being audible, and in the X-Ray picture, there was absorption of much exudate.

On 7. 7. 36. the patient was still working. His weight was 10 st. 11 lbs., no cough or sputum and feeling well.

An X-Ray showed only fibrosis at both apices and there was no clinical evidence of activity.



19. 5. 34.



7. 7. 36.

CASE No. 12.

Female, aged 22 years. Admitted 14. 5. 34.

History of six months cough and sputum with gradual loss of weight. A small haemoptysis one week before admission.

Physical signs: Impairment of percussion over both upper lobes with bronchial breathing and numerous crackling crepitations.

X-Ray: Extensive tubercular infiltrations in both upper lobes with some fibrosis in left upper.

General condition poor. Weight 7 st. 12 lbs.

Sputum - positive. Temperature 98.2°- 99.6°F.

Sedimentation Rate	16.
Polymorphs	74%
Lymphocytes	18%
Mononuclears	8%
Eosinophils	0%

Crisalbin started 22. 5. 34. Dosage: 0.025 gm, 0.025, 0.05, 0.1, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 4. 9. 34. Total 6.05 gm.

General condition had improved considerably; weight increased to 8 st. 4 lbs. Temperature normal. Sputum had decreased in amount and was now negative. Sedimentation rate 9.

A second course was commenced on 16. 11. 34. with the same dosage as course one. Total to 4. 3. 35, 6.05 gm.

Weight had now increased to 8 st. 11 lbs. Temperature normal. Sputum had ceased altogether, although a slight dry cough persisted. The patient was now up eight hours and felt extremely well. Physical signs showed some improvement.

Sedimentation Rate	7.
Polymorphs	70%
Lymphocytes	24%
Mononuclears	4%
Eosinophils	2%

CASE No. 12 (Cont.)

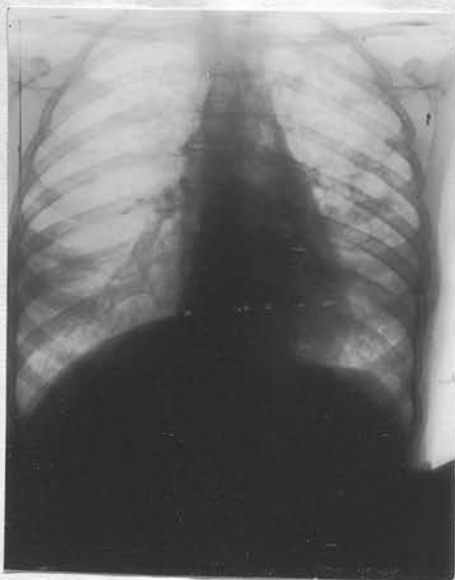
Discharged on 17. 3. 35.

Third course of Crisalbin 20. 5. 35. to 4. 9. 35.
Dosage similar to course one and two, total of 6.3 gm. given.
Weight at end of course 9 st. 4 lbs. Some dry cough still present.

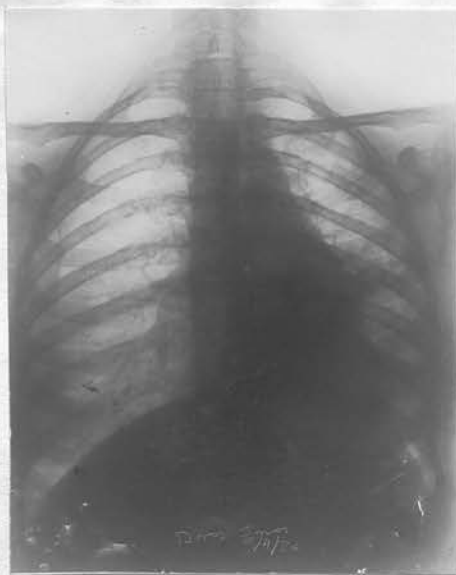
Fourth course of Crisalbin 23. 11. 35. to 2. 3. 36.
Dosage as in course three, total of 6.3 gm. given. Weight now 9 st. 10 lbs, feeling extremely well. No cough or sputum, but some dyspnoea on exertion.

Physical signs: Some impairment of percussion over right upper lobe, breath sounds vesicular, no accompaniments; impairment over left upper lobe with harsh vesicular breathing; no accompaniments.

X-Ray: Right lung clear. Some fibrosis of left upper and lower lobes with traction of mediastinum to the left.



12. 5. 34.



8. 4. 36.

CASE No.13.

Female, aged 23 years. Admitted 19. 6. 34.

History of two months cough, following pleurisy, with loss of weight and feeling of being run down. General condition fairly good. Weight 7 st. 13½ lbs. Sputum positive.

Physical signs: Impairment of percussion over whole of right upper lobe and also left apex. Breath sounds vesicular in both areas but numerous post tussic crepitations audible.

X-Ray: Extensive infiltration in right upper lobe; increase in striae with mottling at left apex. Temperature 98.6°F. in evenings.

Sedimentation Rate	18.
Polymorphs	62%
Lymphocytes	29%
Mononuclears	7%
Eosinophils	2%

Artificial pneumothorax attempted on right side, but failed owing to numerous adhesions.

Course of Crisalbin started on 6. 7. 34. Dosage: 0.025 gm. 0.025, 0.05, 0.05, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals; 0.25 gm. continued twice weekly until 27. 10. 34. Total 6.25 gm.

Sputum reduced from ½ oz. to 1 dram; no tubercle bacilli found.

Weight increased to 8 st. 10 lbs. General condition excellent.

Sedimentation Rate	8.
Polymorphs	64%
Lymphocytes	28%
Mononuclears	4%
Eosinophils	4%

Discharged 20. 11. 34.

CASE No.13 (Cont.)

Weight 9 st. $3\frac{1}{2}$ lbs. No cough or sputum, and feeling extremely well. X-Ray showed considerable absorption of infiltrates in right upper lobe.

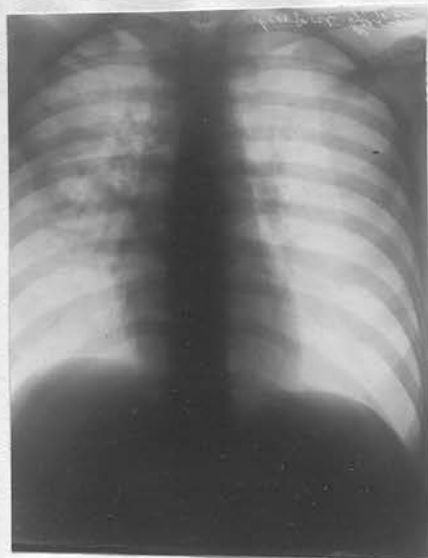
Second course of Crisalbin started 8. 2. 35. Dosage: 0.25 gm twice weekly. Total 5.75 gm; course finished on 22. 5. 35. Weight had increased to 9 st. 8 lbs; no cough or sputum, and doing housework regularly.

Condition on 4. 6. 36.

Weight 9 st. $10\frac{1}{2}$ lbs; feeling extremely well; and working regularly; no cough or sputum.

Physical signs: Impairment and retraction over right upper lobe, some impairment at left apex. Harsh breath sounds at both apices, no accompaniments audible.

X-Ray: Considerable fibrosis in right upper lobe but no radiological evidence of activity; increase in striae at left apex.



22. 6. 34.



4. 6. 36.

CASE 14.

Female, aged 19 years.

This patient was first seen on 17. 5. 34.

History: Lassitude for several months. Cough and spit for past two months and a haemoptysis on 10. 5. 34.

Physical signs: Dullness at left apex with a few fine post tussic crepitations posteriorly.

X-Ray: Subclavicular infiltration in upper left lobe.

General condition poor. Weight 7 st. 6 lbs.

Temperature in evenings 99°F.

Sputum - positive.

She was sent to a private sanatorium on 25. 5. 34. where an artificial pneumothorax was attempted but failed. After this, she had the usual sanatorium regime of rest and graded exercises. She was discharged on 21. 12. 34. and was examined again on 23. 12. 34. The general condition had improved somewhat, the weight now being 7 st. 10 lbs. and the patient felt "a little better". On physical examination, there was considerable spread in the disease in the upper left lobe with cavity formation at the apex.

Sputum - positive.

She was admitted to Holly Lane Sanatorium on 6. 1. 35.

Sedimentation Rate	27.
Polymorphs	73%
Lymphocytes	18%
Mononuclears	9%
Eosinophils	0%

Crisalbin was commenced on 14. 1. 35. Dosage: 0.025 gm. 0.025, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was then continued twice weekly until 25. 4. 35. Total 6.15 gm.

CASE No. 14 (Cont.)

The weight had now increased to 8 st. 1 lb. and the sputum was negative.

The patient was allowed to get up for a short time each day. A second course of Crisalbin, similar to the first, lasted from 19. 6. 35. to 2. 10. 35. Total 6.2 gm.

The general condition was now much better. Weight 8 st. 6 lbs. No cough and no sputum. There was definite improvement in the physical signs and X-Ray picture.

Sedimentation Rate	14.
Polymorphs	67%
Lymphocytes	25%
Mononuclears	6%
Eosinophils	2%

Discharged 10. 10. 35.

A third course similar to the first two lasted from 4. 1. 36. to 16. 4. 36.

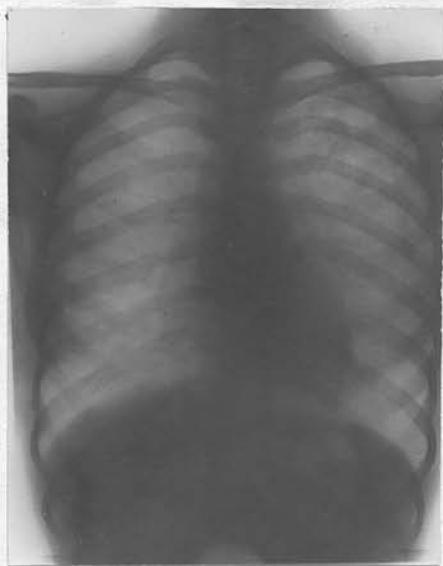
The weight was now 8 st. 13 lbs. No cough or sputum and feeling very well. There was still evidence on physical examination of a cavity at the left apex, but there were no accompaniments audible.

The X-Ray picture had improved considerably. The infiltrations in the left upper lobe had been almost completely absorbed, and there was a thin walled cavity at the apex.

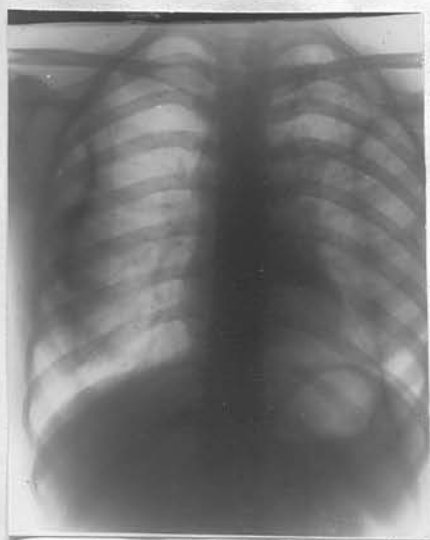
A phrenicectomy was performed on 30. 4. 36.

Another course of Crisalbin was started on 16. 6. 36. and it is proposed that following the completion of this course, a plastic operation be performed to collapse the cavity in the upper lobe.

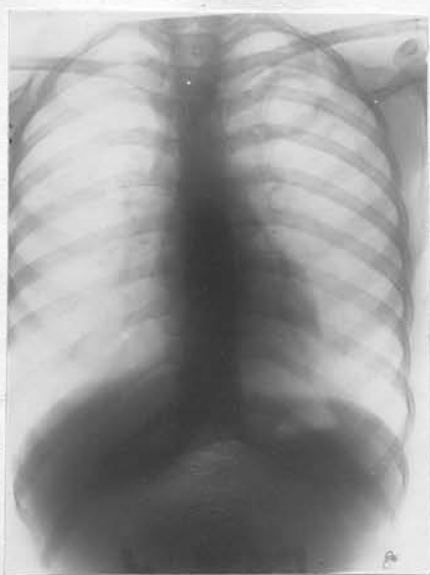
CASE 14.



17. 5. 34.



6. 1. 35.



16. 4. 36.

CASE No. 15.

Male, aged 17 years. Admitted 8. 11. 34.

History of pleurisy six weeks before. Cough had persisted and there was marked lassitude.

General condition poor. Weight 8 st. 8½ lbs.

Temperature 98°- 100°F. Sputum - positive.

Sedimentation Rate	24.
Polymorphs	69%
Lymphocytes	22%
Mononuclears	8%
Eosinophils	1%

Physical sings: Dullness over upper left lobe and upper part of left lower lobe; breath sounds vesicular, numerous fine crepitations. Right apex impaired with a few post tussic crepitations.

X-Ray: Disseminated nodules throughout left lung and right upper lobe.

Crisalbin started 18. 11. 34. Dosage: 0.025 gm. 0.025, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 2. 3. 35. a total of 6.15 gm. being given.

The temperature was now normal and the sputum had become negative. There was still a dry cough, but the general condition had improved greatly. Weight had increased to 9 st. 5¼ lbs.

The patient was allowed up and a second course similar to the first was commenced on 19. 4. 35. and continued to 6. 6. 35. when a rash appeared. The rash was of maculo-papulo squamous type and tended to form large patches on the trunk and extensor surfaces of the arms; it was bright red in colour, but toned down to a dull reddish brown colour. There was no rise of temperature and no malaise. The patches did not fade in the usual way, but tended to become indurated and raised above the level of the surrounding skin. They gradually assumed a yellowish brown colour, and at the time of discharge were present on the front and back of the trunk in patches about two inches in circumference and on the backs of the forearms.

CASE No. 15 (Cont.)

Discharged 14. 8. 35.

Weight 9 st. 8½ lbs. No cough and no sputum.

Sedimentation Rate	12.
Polymorphs	70%
Lymphocytes	24%
Mononuclears	4%
Eosinophils	2%

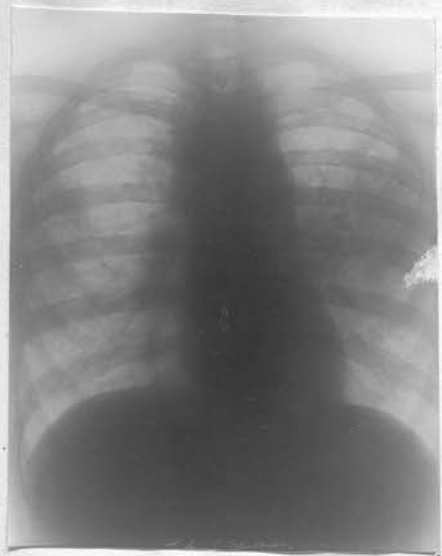
There was definite improvement in the physical signs and the X-Ray picture.

The patient started work on 2. 2. 36. as motor mechanic and has worked steadily since then.

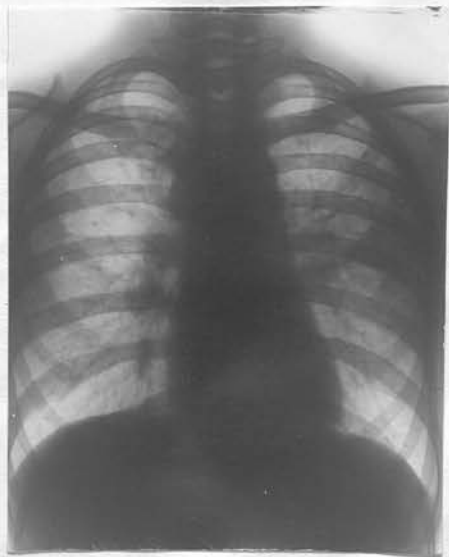
On 7. 7. 36. on physical examination, although dullness existed in the original areas, no accompaniments could now be heard and breath sounds were vesicular in character. Weight was 10 st. 4 lbs. and the patient was feeling very well; no cough or sputum.

The X-Ray showed considerable clearing of the exudations and increase of fibrosis in both lungs.

The rash was still present but much fainter, being now a dirty yellow staining of the skin, and no longer raised.



12. 11. 34.



7. 7. 36.

CASE No. 16.

Female, aged 16 years. Admitted 3. 8. 34.

History of a profuse haemoptysis two days before admission. Had been feeling perfectly well before this, and working without fatigue as a domestic servant; no cough or sputum.

Physical signs: Impairment of percussion over the right upper lobe, breath sounds vesicular with numerous fine crackles; impairment over left apex, with a few post tussic crepitations.

X-Ray: Tubercular infiltration right upper lobe with mottling at left apex.

General condition fairly good. Weight 5 st. 11 $\frac{1}{4}$ lbs.

Sputum - nil. Temperature 98°- 98.6°F.

Sedimentation Rate	14.
Polymorphs	62%
Lymphocytes	24%
Mononuclears	13%
Eosinophils	1%

Crisalbin started 15. 8. 34. Dosage: 0.025 gm, 0.025, 0.05, 0.05, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 1. 12. 34. Total 6.15 gm. being given.

The patient's weight had increased to 6 st. 4 lbs; she was feeling perfectly well, no cough, no sputum, temperature normal. Sedimentation rate 12. She was, however, kept completely at rest in bed and another course was commenced on 27. 1. 35. Dosage was similar to course one, a total of 6.3 gm. being given, finishing on 4. 4. 35. During this course, the patient was gradually allowed up, until at its completion, she was up for eight hours without any reactions.

She was discharged on 16. 4. 35. feeling extremely well. Her weight had now increased to 6 st. 10 lbs; no cough, no sputum.

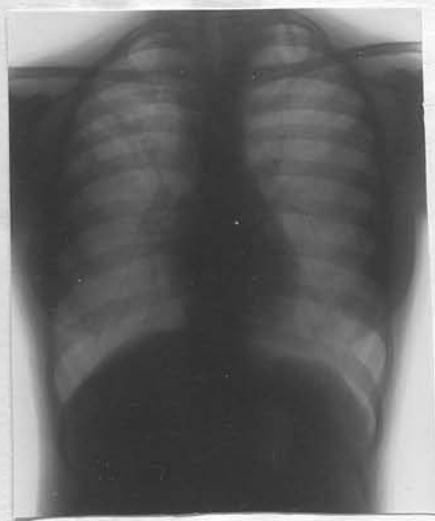
Sedimentation Rate	7.
Polymorphs	64%
Lymphocytes	27%
Mononuclears	6%
Eosinophils	3%

CASE No. 16 (Cont.)

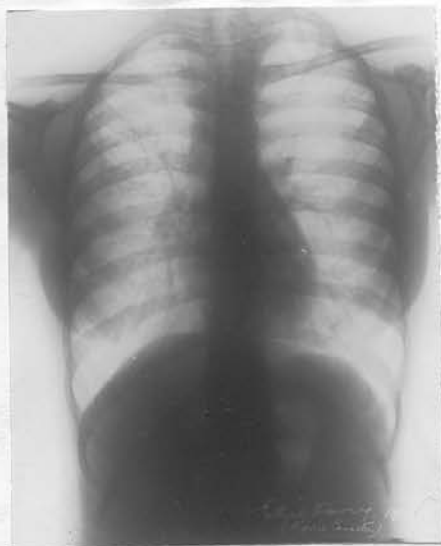
The physical signs had improved, no moisture being now audible in either lung.

X-Ray showed improvement in both lungs.

On leaving sanatorium, patient returned to her home on a farm in Shropshire. On enquiry on 7. 6. 36. the patient reports that she is keeping very well and doing some light housework. She had then no cough or sputum and her weight was 7 st. 4 lbs.



14. 8. 34.



14. 4. 35.

CASE No.17.

Male, aged 24 years. Admitted 4. 8. 34.

History of cough, sputum, lassitude and loss of weight for eight months.

Physical signs: Marked impairment of percussion note over whole of left upper lobe, apex of left lower, and apex of right upper lobe. Signs of cavitation in left upper lobe and many moist sounds throughout lung; breath sounds blowing at right apex, and showers of post tussic crackles throughout right upper lobe.

X-Ray: Extensive infiltrations throughout left lung with cavitation in upper lobe; right upper lobe extensively involved.

General condition very poor. Evening temperature 101°F. Sputum - positive.

Sedimentation Rate	57.
Polymorphs	78%
Lymphocytes	18
Mononuclears	4%
Eosinophils	0%

After three weeks complete rest in bed, the temperature fell to 99°F. in the evening.

Course of Crisalbin started 29. 8. 34. Dosage: 0.025 gm, 0.025, 0.05, 0.05, 0.05, 0.1 gm. at three day intervals. 0.1 gm. was continued biweekly until 29. 10. 34. total 1.3 gm., when an erythematous rash appeared on trunk and limbs, the temperature rising to 100.5 for four days. Treated with Contramine.

The blood count at this time showed a total polymorph percentage of 76 of which 24 per cent were eosinophils. Sedimentation rate was 60.

The rash disappeared in six days, and the temperature settled to 98.2 in the evenings. The weight at this time was 10 st. 3 lbs. Sputum positive.

A rest of a month from injections was given, at the end of which, the polymorph percentage was still 74, but the eosinophils had fallen to 12 per cent.

CASE No. 17 (Cont.)

A dose of 0.025 gm. Crisalbin was then given in 10 cc. Calcium gluconate. The next day the eosinophils had risen again to 22% and the following day an erythematous rash again appeared, with a rise of temperature. This was again treated with Contramine as before, and the temperature settled in two days, the rash persisting this time for six days.

No further Crisalbin was given in this case.

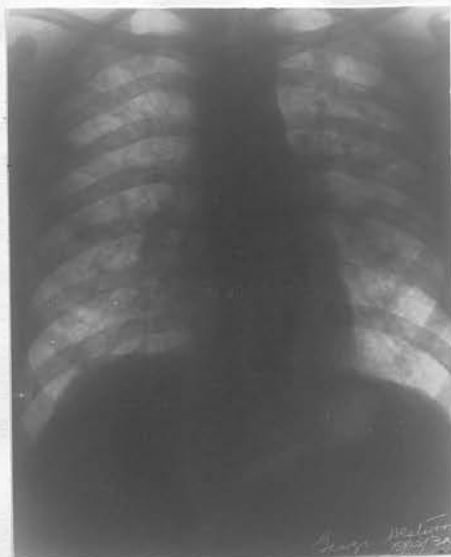
The patient was discharged on 8. 4. 35, at his own request. The weight was then 10 st. 4 lbs; sputum was still positive, and the physical signs showed very little change. The general condition had improved considerably; there was no radiological change obvious.

Sedimentation Rate	48.
Polymorphs	72%
Lymphocytes	16%
Mononuclears	8%
Eosinophils	4%

After discharge, he began to lose weight steadily, his general condition deteriorating rapidly.

On 21. 6. 35. he was only 8 st. 10 lbs. and chest showed new spread of the disease with cavitation in the right upper lobe. Sputum positive.

From that date he was confined to bed at home. His condition continued to deteriorate and he died on 23. 11. 35.



CASE No. 18.

Female, aged 26 years. Admitted 4. 9. 34.

History of "influenza", ten months previously from which she had never fully recovered, having been left with a cough and a tired feeling; during the three months before admission, she had been losing weight steadily, and lately had had a pain in the right side when taking a deep breath.

Physical signs: Signs of extensive consolidation in right upper lobe with cavitation at apex; breath sounds over middle and lower lobes harsh with numerous post tussic crepitations; impairment on percussion at left apex to lower border of second rib with bronchial breath sounds and fine crepitations.

General condition poor. Weight 8 st. 10 lbs.

X-Ray: Extensive tubercular involvement of right upper lobe with cavitation; disseminated disease in middle and right lower lobes; left upper lobe shows mottling above and below clavicle.

Sputum - positive.

Sedimentation Rate	36.
Polymorphes	82%
Lymphocytes	15%
Mononuclears	3%
Eosinophils	0%

Temperature 98° - 99.6°F.

Artificial pneumothorax attempted on right side but a good collapse not obtained owing to wide spread adhesions; it was, therefore, abandoned.

Course of Crisalbin started 11. 10. 34. Dosage: 0.025 gm 0.025, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.025 gm. was continued twice weekly until 4. 2. 35. Total 5.75 gm.

The patient's general condition at the end of the course was if anything slightly worse. Her weight had fallen to 8st. 1½ lbs., her sputum was unaltered in amount and still contained tubercle bacilli.

CASE No. 18 (Cont.)

She had been completely in bed during this period and her temperature had declined, but still tended to rise to 99°F. occasionally in the evening. The sedimentation rate was 40 at the end of the course, and there had been no appreciable alteration in the polymorph, lymphocyte, mononuclear ratio. The physical signs showed some extension of the disease in the left upper lobe and the X-Ray picture was definitely worse than on admission.

After a further period of two months complete rest, a second course of Crisalbin was started. Dosage to commence with was the same as course one, but was increased after four doses of 0.25 gm. to one dose of 0.5 gm. weekly for three weeks, 0.75 gm. weekly for three weeks, and one dose of 1 gm. Following this latter dose the patient developed some stomatitis and diarrhoea, which persisted for a week. Her temperature was settled but her general condition at the end of the course (14. 8. 35) was unaltered. The weight was 8 st. 2 lbs, sedimentation rate 34, blood picture unaltered, sputum positive.

Physical signs showed even more extensive disease in the left lung than previously. The X-Ray picture showed extension of the disease in both lungs.

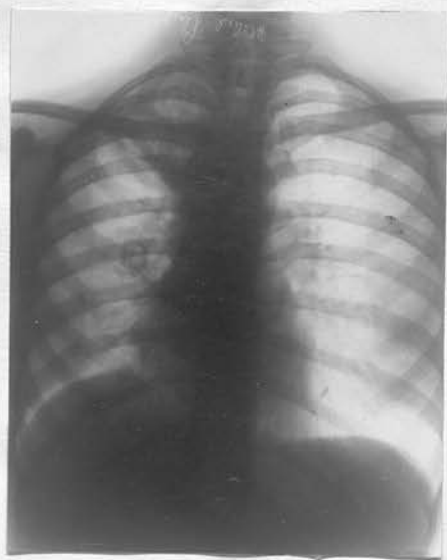
The patient was discharged on 4. 10. 35. at her own request. Her weight was then 8 st. 3 lbs.

Sedimentation Rate	32.
Polymorphs	73%
Lymphocytes	17%
Mononuclears	10%
Eosinophils	0%

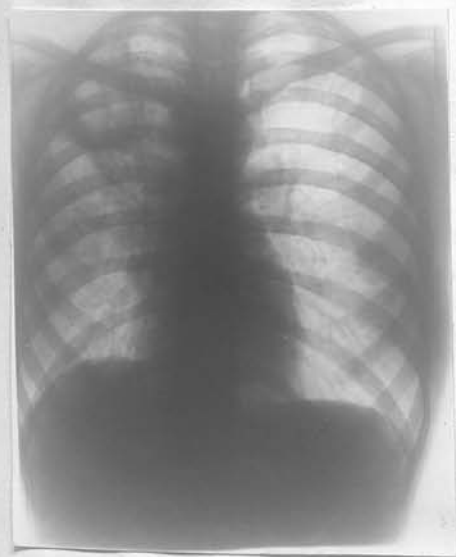
On returning home her condition grew steadily worse. She lost weight, suffered from occasional attacks of diarrhoea, and in January 1936. became very hoarse. There was tenderness over the ascending colon, and undoubtedly an intestinal tuberculosis was present.

The patient died on 18. 3. 36.

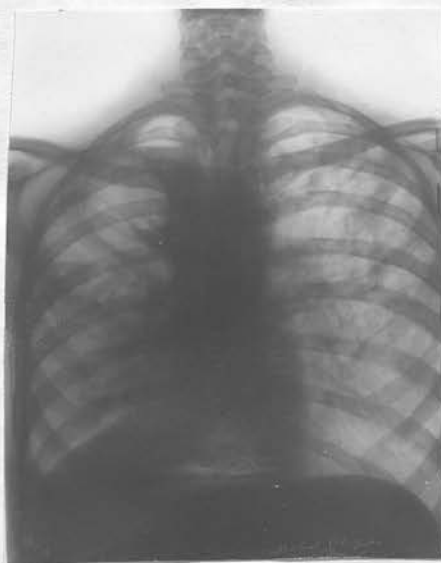
CASE 18.



6. 9. 34.



8. 2. 35.



18. 12. 35.

CASE No. 19.

Female, aged 17 years. Admitted 1. 5. 34.

History of 'Influenzal attack' three months previously which had left patient feeling very weak. She had lost weight steadily and had a very troublesome cough with scanty sputum.

Physical sings: Signs of extensive tubercular involvement of both upper lobes.

X-Ray: Tubercular infiltrations throughout both upper lobes with early cavitation.

General condition very poor. Weight 6 st. 9½ lbs.

Sputum - positive. Temperature 98° - 100.4°F.

Sedimentation Rate	28.
Polymorphs	67%
Lymphocytes	21%
Mononuclears	10%
Eosinophils	2%

Crisalbin started 5. 5. 34. Dosage: 0.025 gm, 0.025, 0.05, at three day intervals. A febrile reaction lasting two days followed the third dose; a weeks interval was, therefore given, followed by 0.025 gm, 0.025, 0.025, 0.05, 0.05, 0.1 gm, again at three day intervals. Another febrile reaction, shorter than the first, followed the dose of 0.1 gm. After another week, dosage was recommenced again at 0.025 gm, and increased to 0.25 gm, without further incident. This dose was continued twice weekly and 6.025 gm. had been given. The course lasted till 30. 10. 34. The patient's general condition was definitely better. Weight had increased to 7 st., and the sputum had become negative. The temperature was normal, the patient being at rest in bed. The sedimentation rate had fallen to 22.

Two months rest was allowed, the patient still being at complete rest in bed, and then another course was given, starting on 2. 1. 35. Dosage: Starting at 0.025 gm, dosage was increased gradually to 0.25 gm, with three day intervals, there being no reactions. A total of 6 gm. was given. The general conditon had improved considerably, weight on 14. 4. 35. at the end of the second course, being 7 st. 7 lbs. Sputum had ceased and there was only a slight dry cough. The X-Ray picture had improved considerably.

CASE No. 19 (Cont.)

Sedimentation Rate now	10
Polymorphs	64%
Lymphocytes	27%
Mononuclears	6%
Eosinophils	3%

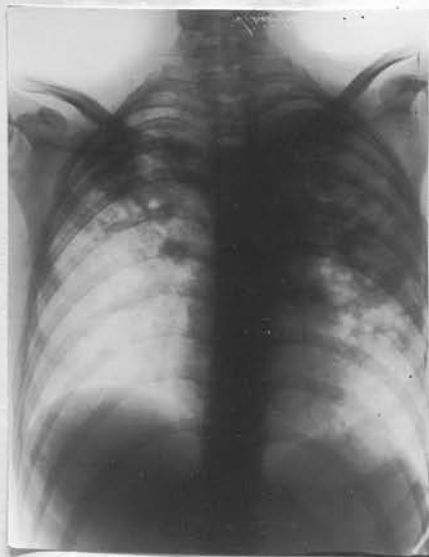
Temperature - normal.

The patient was now allowed up, and was discharged on 27. 7. 35.

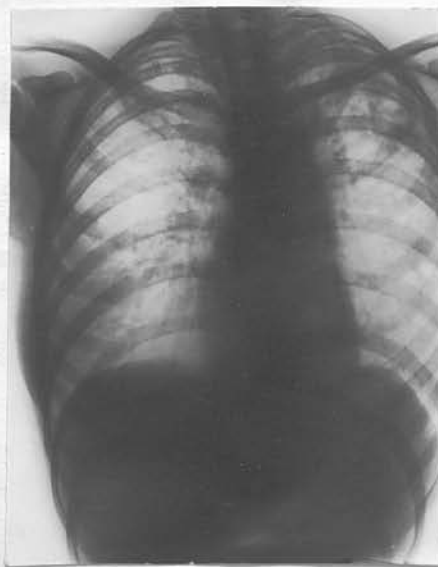
A third course of Crisalbin was started on 2. 9. 35. Dosage: 0.025 gm, increasing steadily to 0.25 gm, this dose being continued twice weekly until 18. 12. 35, a total of 5.5 gm. being given. The patient was now 8 st. 1 lb. and was feeling extremely well. Slight dry cough still persisted.

A fourth course with dosage similar to the third, was commenced on 4. 2. 36. and finished on 24. 5. 36. The patient's weight was now 8 st. 12 lbs. Slight morning cough persisted, but no sputum and she felt very well indeed, being able to walk five miles per day with no feeling of exhaustion.

The X-Ray picture showed considerable absorption of the infiltrations in both lungs, and a considerable amount of fibrous tissue formation taking place.



8. 5. 34.



27. 6. 36.

CASE No. 20.

Female, aged 18 years. Admitted 31. 9. 34.

History of four months cough, spit and lassitude.

Physical signs: Signs of extensive disease throughout both lungs, more marked on the left side.

X-Ray picture showed extensive lesions in both lungs, with some fibrosis on left side and traction of mediastinum to that side.

General condition poor. Weight 7 st. 2 lbs.

Sputum - positive. Temperature 98°- 98.8°F.

Sedimentation Rate	42.
Polymorphs	70%
Lymphocytes	17%
Mononuclears	12%
Eosinophils	1%

Crisalbin started 14. 10. 34. Dosage: 0.025 gm. 0.025, 0.05, 0.05, 0.1, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly. After a total of 1.9 gm. had been given, a scarlitinaform rash appeared which lasted six days. Two weeks rest was given and the course recommenced with doses of 0.025 gm. There were no further reactions and the course was finished on 26. 2. 35, a total of 6.305 gm. having been given.

The general condition was improved and the patient felt much better; the temperature was normal but the pulse rate varied between 90 and 100 at rest in bed. The physical signs were unchanged and the X-Ray picture showed further spread of the disease. Sedimentation rate 39. Cough was still present and the sputum was still positive.

Patient was kept at complete rest and a second course of Crisalbin was started on 17. 4. 35. Dosage: 0.025 gm. 0.05, 0.05, 0.1, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. twice weekly was then continued for four weeks. 0.5 gm. was then given weekly for four weeks and 1.0 gm. weekly for two weeks. Total to 14. 8. 35. 6.775 gm.

Weight had now increased to 7 st. 13 $\frac{1}{4}$ lbs. Cough was still present but sputum had ceased.

CASE No. 20 (Cont.)

Temperature normal but pulse still varied between 90-100.

Sedimentation Rate	35.
Polymorphs	69%
Lymphocytes	22%
Mononuclears	8%
Eosinophils	1%

X-Ray picture showed still further extension of the disease in both lungs. There was remarkably little systemic reaction when the extent and spread of the disease was considered.

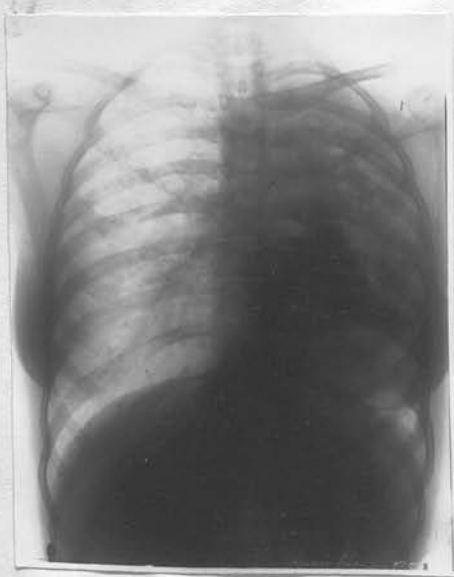
Discharged 26. 8. 35.

After two months at home, the weight had fallen to 7 st. 8 lbs. and sputum had returned, and contained tubercle bacilli.

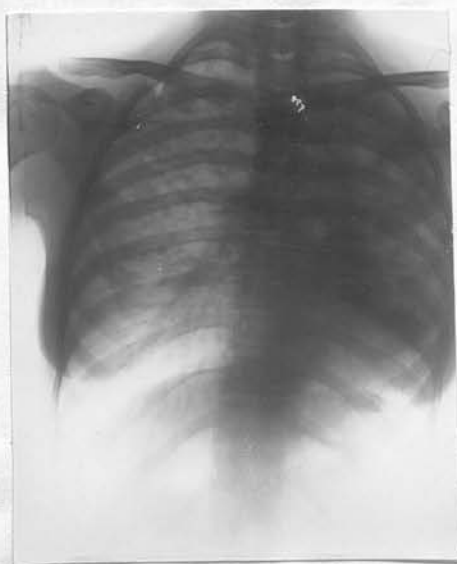
A third course of Crisalbin similar to course two was given from 9. 11. 35. to 4. 3. 36. Total 6.775 gm.

The weight had now fallen to 7 st. $\frac{1}{4}$ lb. There was further radiological evidence of extension of the disease and lassitude was marked. In spite of this, there was no temperature, but the pulse rate averaged 110.

From 5. 4. 36. the patient was confined to bed, and continued to waste steadily. She died on 13. 7. 36.



2. 10. 34.



29. 2. 36.

CASE No. 21.

Male, aged 41 years. Admitted 24. 5. 34.

History of cough, "wheezing" and some sputum for seven months; loss of weight and lassitude during past eight weeks.

Physical signs: Impairment of percussion over whole of right upper lobe and right apex to upper border of second rib. Breath sounds harsh vesicular; numerous moist sounds at both apices.

X-Ray: Tubercular fibrosis both upper lobes, more marked on right side.

Weight 7 st. 12 lbs. General condition poor.

Sedimentation Rate	17.
Polymorphs	70%
Lymphocytes	22%
Mononuclears	5%
Eosinophils	3%

Sputum - positive. Evening temperature 98.4°F.

Crisalbin started 5. 6. 34. Dosage: 0.025 gm, 0.05, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. continued twice weekly until 27. 9. 34. Total 6 gm.

General condition improved steadily. Sputum became negative on 20. 8. 34. and was absent altogether by the end of the course. Cough also disappeared and the weight increased to 9 st. 2½ lbs. No moisture now audible in either lung.

Sedimentation Rate	4.
Polymorphs	68%
Lymphocytes	26%
Mononuclears	4%
Eosinophils	2%

Discharged 18. 10. 34.

Started work again on 7. 1. 35. and has worked regularly ever since, as a mechanic.

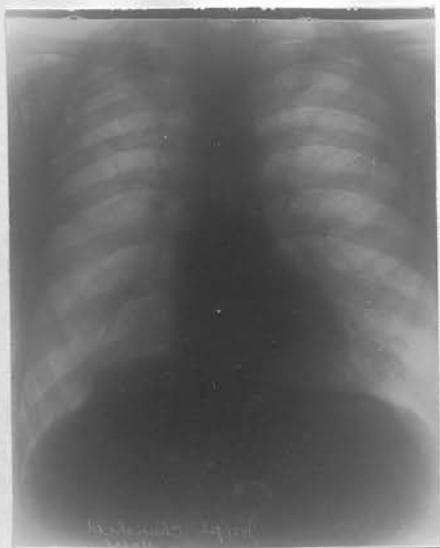
Second course of Crisalbin given from 2. 3. 35. to 10. 6. 35. Dosage: 0.25 gm. twice weekly. Total 6.5 gm.

CASE No. 21 (Cont.)

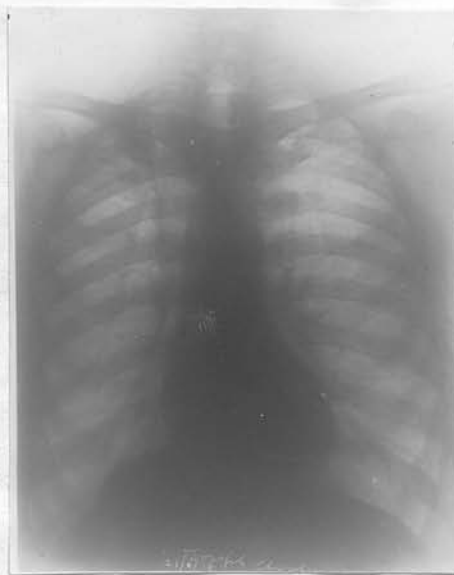
Has remained well since discharge. On 21. 4. 36. the general condition was excellent; weight 9 st. 8 lbs; no cough or sputum; slight dyspnoea on exertion but otherwise felt very well.

Physical signs: Impairment and retraction over right upper lobe; some impairment at left apex. Breath sounds harsh vesicular; no accompaniments.

X-Ray: Increased fibrosis in both upper lobes; no radiological evidence of activity.



4. 6. 34.



21. 4. 36.

CASE No. 22.

Male, aged 34 years. Admitted 18. 1. 35.

History of six months cough, sputum, loss of weight, lassitude, night sweats and dyspnoea.

Physical signs: Signs of extensive fibro caseous disease in both lungs.

X-Ray: Extensive tubercular involvement both lungs with cavitation at left apex.

Sputum - positive.

General condition poor. Weight 9 st. 7 lbs. Evening temperature 100 to 100.6°F.

Sedimentation Rate	58.
Polymorphs	75%
Lymphocytes	18%
Mononuclears	7%
Eosinophils	0%

Crisalbin started 30. 1. 35. Dosage: 0.025 gm, 0.025, 0.05 0.05, 0.1, 0.1, 0.15, 0.15, 0.15, 0.25 gm. at three day intervals. 0.25 gm. continued twice weekly until 3. 4. 35; total amount given 6.15 gm.

Temperature became more settled, but still tended to rise occasionally to 98.8°F. in the evening. Weight increased to 9 st. 13 lbs. but there was no real improvement in the general condition. Sputum remained unchanged in amount and in bacillary content.

Discharged 19. 6. 35.

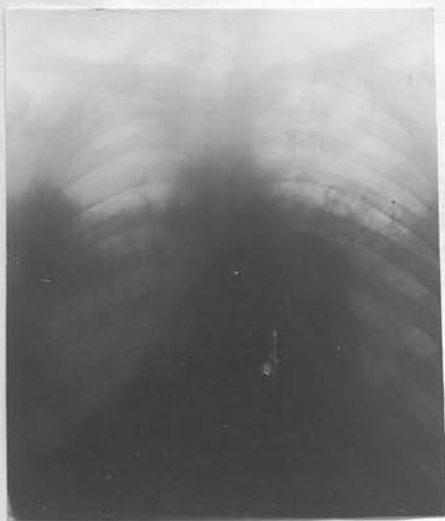
Sedimentation Rate	40.
Polymorphs	72%
Lymphocytes	22
Mononuclears	6%
Eosinophils	0%

X-Ray: No improvement in lung condition seen.

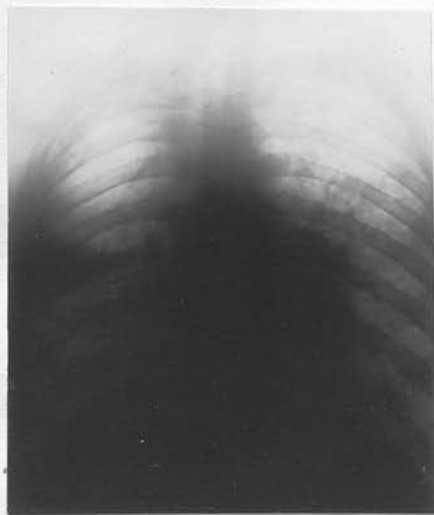
Second course of Crisalbin commenced 22. 7. 35; general condition had deteriorated since discharge and weight was now 9 st. 4 lbs., but readmission to sanatorium was refused.

CASE No. 22 (Cont.)

Dosage: 0.15 gm, 0.15, 0.25. twice weekly; 0.25 gm. continued twice weekly for a month - total given 2.55 gm. It was obvious this patient was going quickly down hill; he was confined to bed at home on 31. 8. 35, again refusing sanatorium. His condition grew steadily worse and he died on 25. 1. 36.



5. 2. 35.



18. 6. 35.

CASE No. 23.

Male, aged 44 years. Admitted 9. 10. 34.

History: First diagnosed as suffering from pulmonary tuberculosis in 1925. Fibroid type of case and had remained well, although troubled with a dry cough, and shortness of breath. During the past six months he had begun to lose weight and suffer from lassitude. Recently had begun to have a spit as well as a cough.

Physical signs: Signs of old standing bilateral disease with cavitation at left apex. Signs of activity in both upper lobes.

General condition poor. Weight 9 st. $\frac{1}{4}$ lb.

Temperature 97.8° to 99.4°F.

Sputum - positive.

X-Ray: Old standing tubercular fibrosis of both lungs with cavitation at left apex; more recent infiltrations in middle zone of left lung and in right upper lobe.

Sedimentation Rate	22.
Polymorphs	74%
Lymphocytes	18%
Mononuclears	4%
Eosinophils	4%

A course of Crisalbin was started on 18. 10. 34. Dosage: 0.025 gm. 0.025, 0.05, 0.1, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was then continued until 9. 1. 35. when diarrhoea developed. This settled down within three days. Total given 4.2 gm.

The temperature was now settled; weight had increased to 9 st. 6 lbs. and the sputum was negative.

The patient was allowed up and a second course of Crisalbin was started from 2. 3. 35. to 13. 6. 35. Dosage similar to course one, a total of 6.15 gm. being given. The physical signs were somewhat improved and the X-Ray picture showed some slight improvement. Sputum negative.

Sedimentation Rate	11.
Polymorphs	70%
Lymphocytes	22%
Mononuclears	4%
Eosinophils	4%

CASE No. 23 (Cont.)

Discharged 20. 6. 35.

Third course of Crisalbin 18. 8. 35. to 2. 12. 35.
Dosage similar to courses one and two, a total of 6.15 gm.
being given.

At the end of the course the weight was 10 st. 2 lbs.
Cough was still present, but the sputum had ceased, and
the patient was feeling very well. He returned to work
as a clerk on 1. 2. 36. and has been working ever since.

On 17. 6. 36. the weight was 10 st. 4 lbs. No sputum
present and feeling very well.

The physical signs still showed some activity at both
apices, but were much improved.

X-Ray showed some slight increase in fibrosis.



20. 10. 34.

CASE No. 24.

Female, aged 43 years. Admitted 26. 11. 34.

History of chronic cough for years. During last six months, patient had left run down and had lost nearly a stone in weight. Sputum had been copious during last few months.

Physical signs: Impairment of percussion over both upper lobes with signs of cavitation at left apex; numerous coarse crepitations throughout both upper lobes.

X-Ray: Extensive tubercular fibrosis of both upper lobes with cavitation in left upper.

General condition fairly good. Weight 7 st. 8 $\frac{1}{4}$ lbs.

Sedimentation Rate	16.
Polymorphs	67%
Lymphocytes	23%
Mononuclears	10%
Eosinophils	0%

Sputum - positive. Temperature 97°- 98.8°F.

Crisalbin started 2. 12. 34. Dosage: 0.025 gm, 0.05, 0.1, 0.15, 0.25 gm. at three day intervals. 0.25 gm. was continued twice weekly until 14. 3. 35. Total 6.15 gm.

Sputum had decreased in amount and was now negative. Weight had increased to 8 st. 3 lbs. Sedimentation rate 13.

Patient was allowed up and a second course of Crisalbin was started on 7. 5. 35. This was similar to course one and finished on 28. 8. 35. Total 6.15 gm.

Patient was feeling very well. Cough was not troublesome and sputum was less, mucoid, and negative.

Sedimentation Rate	9.
Polymorphs	66%
Lymphocytes	28%
Mononuclears	5%
Eosinophils	1%

Weight had increased to 8 st. 7 lbs.

CASE No. 24 (Cont.)

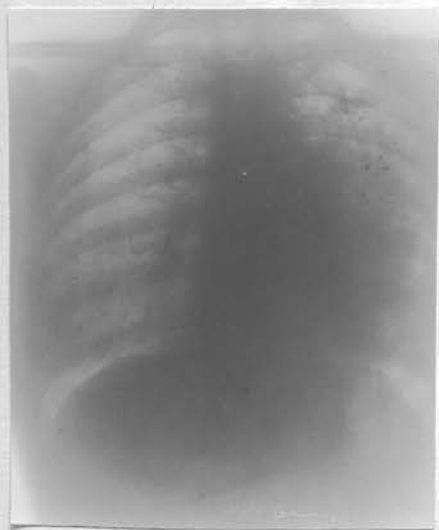
Discharged 4. 9. 35.

Third course Crisalbin 2. 2. 35. to 16. 5. 35. Dosage similar to courses one and two; total 6.15 gm.

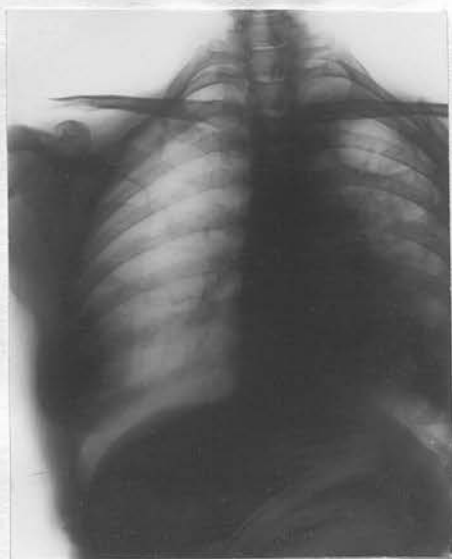
Weight now 8 st. 10 lbs. Cough not troublesome, sputum negative, feeling very well, and doing her housework regularly.

Physical signs showed considerable improvement.

X-Ray: Extensive tubercular fibrosis throughout left lung; some increase in fibrosis in right upper lobe.



30. 11. 34.



4. 6. 36.

RESULTS OF TREATMENT.

(a) Cases treated by artificial pneumothorax and Crisalbin.

There are seven cases in this group, Nos. 1 to 7 in the series. Three of these, Nos. 1, 4 and 7, had bilateral disease when first they came under treatment. All have shown improvement and in none has there been any spread of disease in the uncollapsed lung. In the case of No.1, all evidence of active disease in the contralateral lung has disappeared leaving only some scarring seen on radiological examination. The pneumothorax in this case is still being carried on, but the patient has been doing hard work for more than a year and his condition and muscular tone are excellent.

Case No. 4. has also lost all evidence of active disease in the contralateral lung. Her artificial pneumothorax is also being carried on.

Case No. 7. is one of a very young girl with a spreading type of disease in both lungs. Whilst the ultimate prognosis in this case must still remain very doubtful, there is no question but that she has obtained considerable benefit from gold therapy. The disease in the uncollapsed lung has not spread, but indeed has shown a tendency to absorption. This is the

type of case which without treatment one would expect to proceed fairly rapidly to a fatal end, and it seems very gratifying that the patient should have improved so considerably, even although the future must remain as yet uncertain.

Cases Nos. 2, 3, 5 and 6 were all unilateral when first seen and were treated primarily by artificial pneumothorax, but all had a subsequent spread of the disease to the uncollapsed lung. Nos. 3 and 6 have since had their pneumothorax treatment discontinued and both are working, the former earning her living in a factory and the latter doing housework. In neither is there any evidence of active disease in the lung which was collapsed or in the contralateral lung.

Cases 2 and 5 have not such a fortunate history as the others in this group. Case 2 had a spread of disease to the contralateral lung subsequent to the collapse of the one originally infected, and the disease then continued to spread in both lungs. Absolutely no benefit was shown from gold therapy in this case which had a fatal termination. The patient came of very bad stock and had been exposed to massive infection in the house, both her father and elder sister being cases of open pulmonary tuberculosis with positive sputa.

Case 5 has a like history, the subsequent spread of disease to the uncollapsed lung being quite unaffected by gold therapy and necessitating the abandonment of the pneumothorax treatment. Subsequent courses of gold injections had likewise no effect, and a fatal termination of this case is only a matter of time.

In five out of seven cases, therefore, gold therapy has controlled a spread in the uncollapsed lung and in four of these, all evidence of such active spread has disappeared. One case of this group is dead, and one is worse.

(b) Cases of fresh spreading exudative disease treated by Crisalbin alone.

In this group, there are thirteen cases, Nos. 8 to 20. All the patients were young and all, with one exception (Case 14), had bilateral disease. In two other cases, Nos. 13 and 18, the extent of the disease in the better lung did not preclude collapse of the worse lung, but in all three cases, artificial pneumothorax treatment failed owing to numerous adhesions, and gold therapy had to be fallen back upon as the first line of treatment.

Cases 10, 11 and 12 were a mixture of nodular productive, and exudative lesions, all the others in this group were purely exudative. Cases 17, 18, 19 and 20

were very widespread lesions and the patients were exceeding toxic when they first came under observation.

Cases 8 and 9 bear a close resemblance to each other clinically. Both had a bilateral apical involvement with basal annular shadows. Both cases have shown a steady improvement in the apical condition until now no evidence of active disease in these areas remains. The annular shadows however, still persist in both cases, but now the condition is amenable to collapse therapy either in the form of artificial pneumothorax or localised thoracoplasty combined with phrenicectomy if necessary. In both cases, however, the patients are quite symptomless and both are working without any ill effects, so that it is felt a further period of observation is justified before deciding on any radical form of treatment.

The productive and exudative cases, (Nos. 10, 11 and 12) have all responded in a most satisfactory way to treatment, and all three have shown absorption of exudate and transformation of the productive lesions into fibrous tissue in a most marked degree.

Cases 13 and 15 have likewise shown an absorption of exudate and formation of fibrous tissue to an extent only slightly less marked than that of the preceding three cases.

Case 14 has responded to treatment in a way which has altered her whole prognosis. In spite of the fact that a large cavity was present at the apex of one upper lobe, the exudative disease in the surrounding lung tissue has undergone resolution and enabled a thoracoplastic operation to be considered in order to obliterate the cavitation. The patient's improved condition and the type of local lesion remaining, make the results to be expected from such a procedure, most hopeful. Before gold therapy was instituted, the course had been a downward one in spite of routine sanatorium treatment.

Case 16 has also given a good functional result, for the patient is at the time of writing, quite symptom free. Actual clinical and radiological examination of this case during the past year, however, has not been possible.

The last four cases in this group, Nos, 17, 18, 19 and 20, were as stated above, widespread lesions with considerable toxaemia. In one of these (No. 19), the improvement has been extraordinary, and dramatic. The widespread lesions from which this case was suffering when she first came under observation, have to great extent disappeared leaving only slight traces of their presence.

This patient is still improving to an extent which it is impossible to believe would have been obtained without the help of gold therapy.

Cases 17, 18 and 20 showed absolutely no benefit from the treatment and the disease progressed steadily and without remission in spite of repeated courses of gold injections. All three cases ended fatally.

The results in this group then are, one case improved, nine considerably improved, and four dead.

(c) Chronic fibro-caseous cases treated with Crisalbin.

This group comprises four cases, Nos. 21 to 24.

Cases 21 and 22 both gave a comparatively short history of symptoms, but their lesions were such that it was obvious the disease was of very old standing and that the symptoms complained of were in the nature of an exacerbation superadded to an old standing process.

Cases 23 and 24 had had symptoms for years but these had been worse for a few months before coming under observation.

The lesions in case 21 were mainly fibrous in character, and although the patient improved considerably under treatment, it is doubtful how much was due to the gold therapy, as this is the type of case which usually does so well under a simple sanatorium regime.

The same applies to cases 23 and 24, although in both those cases cavitation was present. The most outstanding feature about these three cases was the diminution in the quantity and bacillary content of the sputum. All three were rendered sputum negative.

In the case of No. 22, the treatment was of no benefit whatsoever. This case was definitely more advanced and of a more severe and toxic nature than the other three, but gold therapy did not improve his condition in the slightest and his progress was steadily downhill to a fatal termination.

The results in this group are, therefore, three patients improved and one dead.

SUMMARY OF RESULTS.

	No. of Cases.	Improved.	Very much Improved.	Worse.	Dead.
Cases treated by A.P. & Crisalbin.	7	1	4	1	1
Exudative Cases treated with Crisalbin alone.	13	1	9	-	3
Fibro-caseous Cases treated with Crisalbin.	4	3	-	-	1
	24	5	13	1 or 5%	5 or 20%

75%

Effect of Gold Treatment upon the Sputum.

One of the most noticeable effects of treatment was the reduction in the quantity and in bacillary content of the sputum. The first effect usually noticed was that the sputum became clearer and more mucoid in character. In many cases it disappeared altogether.

Of the twenty four cases treated, twenty three had originally tubercle bacilli in their sputum. Of these twenty three, seventeen or 74% became negative, and have had no return of bacilli to their sputum since.

Effect on the X-Ray Picture.

Marked changes in the X-Ray pictures especially of Groups 1 and 2 were seen. This was more noticeable in Group 2, the exudative type of cases. Here there was seen absorption of infiltrates and new formation of fibrous tissue. This latter was most noticeable in cases 10, 11 and 12, the more nodular type. Here the new fibrous tissue formation was considerable and more marked than one is accustomed to seeing in cases not so treated.

In the fibro-caseous group, changes in the X-Ray picture were not so noticeable, as in the first two groups or of such significance with regard to the ultimate prognosis.

Effect of Gold Treatment on the Blood.

The work of Medlar (106), Doan and Sabin (107, 108) has stressed the significance of the relative numbers of the "three key cells" (monocytes, lymphocytes and neutrophiles). The position is summarised by Briskman (109) as follows: An increase in monocytes with a drop in lymphocytes, and increased "shift to the left" indicates an active progressive lesion. The lymphocytes increase with healing and decrease as the disease progresses; they are an indication of healing. The neutrophile is the essential cell in the formation of the uncontaminated tuberculous abscess. An early change following infection is the disappearance of the eosinophiles. When recovery is about to take place (1) Eosinophiles reappear; (2) the lymphocytes and monocytes increase and the neutrophiles decrease; (3) the disproportion between the "three key cells" returns to normal.

In the present series, the blood changes were found to approximate very closely to the clinical condition of the patient. In conjunction with the clinical examination of the patient they formed a valuable aid in the forming of a prognosis. They improved *pari passu* with the clinical condition and

gold treatment did not appear to exert any specific effect upon the blood picture.

Where sanocrysin rashes appeared (Cases 17 and 20) there was a marked eosinophilia, (20 to 30%) This actually preceeded the rash in Case 17.

In Case 15 where the rash was of a different type to the usual sanocrysin reaction, there was no eosinophilia.

The sedimentation rate was another very useful aid to prognosis. All the fatal cases in this series had a very high initial sedimentation rate. One case, however, (No. 8) had an original sedimentation rate of 48, and yet made steady progress and has given a very satisfactory result. The sedimentation rate in this case improved as the patient improved and this was found throughout the series. The value of the test appears to be not in one isolated examination, but in frequently repeated tests, which will show a steady decline in rate with genuine improvement of the pathological condition. Where the sedimentation curve appeared to differ from the rest of the clinical examination, it never proved to be very far wrong in its prognostic value.

TOXIC REACTIONS.

Very few undesirable reactions occurred. Not one case in the series showed any signs of renal damage. No albuminuria was encountered and microscopical examination of the urine also gave consistently negative results in spite of careful and repeated examinations at regular intervals.

Three cases developed skin rashes. In Cases 17 and 20 these took the form of scarlatinial rashes on trunk and limbs. This was accompanied in both cases by intense itching, malaise, a rise in temperature, and marked eosinophilia. In Case 17 after a rest from treatment, a further dose occasioned a recurrence of the rash and eosinophilia. Under the circumstances it was thought wiser to stop further injections.

In Case 20, injections were continued after two weeks rest and no further reactions were encountered.

In Case 15, the rash was entirely different from the usual skin reactions. It at first presented an appearance simulating a very acute psoriasis, and was associated with itching, but no general reaction or eosinophilia. Its subsequent course was entirely unlike a psoriasis, however, and although not resembling

"Chrysiasis" the suggestion of actual deposition of gold in the skin could not be dismissed from the mind, although actual proof of this is of course not to be had.

Two cases (18 and 23) suffered from diarrhoea and one of these (18) had in addition, stomatitis.

Following a short rest from treatment these symptoms quickly settled down in both cases.

Febrile reactions were encountered in one case only (19). This case was initially very toxic and a febrile reaction lasting a week and associated with general malaise and headache followed the third dose (0.05 gm). Another and shorter reaction also with general symptoms followed a dose of 0.1 gm. With a rest from treatment and a reversion to a smaller dose, it was found that the tolerance increased and larger doses could be given with no reaction. A very noticeable result of these two reactions in this case was a decided improvement in the temperature chart and general clinical condition. This is probably in the nature of a "shock" reaction, and must always be a two edged weapon, and not one which it is advisable to aim at, especially in a case such as this with widespread exudative lesions and marked toxæmia. The ultimate result of this case, however, has been spectacular in its success.

DOSAGE.

The doses employed in this series have been according to the standards of most authors, small. In only three cases has a dose of 0.25 gm. been exceeded, (Nos. 5, 18 and 20), and in these three, larger doses failed to influence the course of the disease just as had the smaller.

It would appear from this series, therefore, that favourable results are obtained in suitable cases with small doses, and where these fail to produce improvement, larger doses will also fail.

The small number of toxic reactions in this series appears to be an added argument in favour of small dosage.

CONCLUSIONS.

1. Gold therapy is of definite value in the treatment of pulmonary tuberculosis.
2. Its results cannot compare with those of collapse therapy, but it makes artificial pneumothorax possible in many cases of bilateral disease where otherwise it would be precluded by the nature and extent of the lesion in the contralateral lung.

In originally unilateral disease treated by artificial pneumothorax it can control a new spread in the contralateral lung which would otherwise necessitate the abandonment of the collapse.

3. In unilateral exudative disease where artificial pneumothorax has been tried and failed, it may so influence the course of the lesions as to bring about a condition suitable for thoracoplasty.
4. It is in freshly spreading exudative or nodular lesions that its beneficial influence is most apparent. Exudative lesions undergo absorption and the productive nodular type, fibrosis to an extent which is not usually seen in cases treated by sanatorium regime alone.

5. Exacerbations in the course of chronic fibro-caseous disease may be favourably influenced. Here again it is the fresh spreading disease which is mainly affected.
6. The consistence, quantity and bacillary content of the sputum are all favourably influenced and in a large proportion of treated cases, the sputum becomes, and remains negative.
7. Small doses not exceeding 0.25 gm. give just as favourable results as larger ones, and the undesirable reactions likely to result from the use of gold therapy are milder and much less frequent with small rather than with large doses.
8. When small doses do not influence the course of the disease in a favourable manner it is unlikely that an increase in the size of the dose above 0.25 gm. will have any beneficial results.

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